Perception of differences between pairs of tablets

As an exercise with students in clinical pharmacology, we did visual comparisons of pairs of tablets to detect differences. The objective was to demonstrate the necessity of manufacturing exactly similar placebo tablets for clinical trials. One hundred and nineteen students (86 physicians and 33 pharmacists) took part. They were asked to compare pairs of tablets in small boxes seen during a limited time. Students were divided in groups of six (plus one group of five). Each group received a randomized block of six numbered boxes containing pairs of tablets of three types (a) white, round, flat; (b) yellow, round, convex; (c) pink, oblong, convex. Each type of tablets had been prepared in two forms differing only by the pressure rate and therefore having a slightly different rough surface. Pairs of tablets exactly similar or slightly different were stuck at the bottom of small plastic boxes bearing numbered codes. Three times at signals, each student opened and closed one box and then exchanged it with the student next to him in the group. The three boxes were examined for 1s, 5s and 30s, respectively (there were therefore $119 \times 3 = 357$ answers). The only questions asked were: 'different or similar tablets' and corresponding number of box.

Results were tested with chi-square and G tests. Blindness was broken at the end of the session by distributing the code to all groups. The test detected no difference between physicians and pharmacists ($\chi^2 = 0.28$; $P = 0.87$); between students with correct (102) or unsatisfactory (17) vision ($\chi^2 = 0.18$; $P = 0.9$); there were no differences on the total number of errors according to time: 36, 37 and 39 with 1, 5 and 30 s examination respectively, but great difference as to the type of error: respectively 37, 24 and 15 'different pairs perceived as similar', and 12, 13 and 24 'similar pairs perceived as different' ($\chi^2 = 24$; $P = 0.0005$). The response was influenced by the type of tablets: 31, 49 and 45 errors respectively for white, yellow and pink tablets ($\chi^2 = 7.3$; $P = 0.03$). Irrespectively of true answer, white tablets were found more often similar (78 times) than yellow (71) or pink (49): $\chi^2 = 13.6$; $P = 0.001$.

This 'class-room' experiment was welcomed by the students as it provided interesting opportunities to discuss double-blindness, and matching placebo. Increased perception of differences with time of examination looked interesting although foreseeable.

Finally, the fact that slight differences due to compression force were less apparent in white flat tablets than coloured and convex ones seems to give an interesting indication for double-blind trials.

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Impaired enzyme induction by rifampicin in the elderly

The pharmacokinetic factors contributing to the high incidence of adverse drug effects in the elderly include reduced hepatic biotransformation by microsomal mixed function oxidase enzymes in this age group (O'Malley *et al.*, 1971; Crooks *et al.*, 1976; Greenblatt *et al.*, 1982).

Animal studies have demonstrated an age-dependent decrease in the activity of microsomal oxidative enzymes and the extent to which they can be induced (Kato *et al.*, 1964; Kato & Takanaka, 1968; Adelman, 1975). Salem and his colleagues (1978) found no evidence of enzyme induction in six elderly patients who had been treated with dichloralphenazone, yet enzyme induction assessed by enhanced clearance of quinine and antipyrine was evident in a group of six younger subjects following exposure to identical doses of dichloralphenazone for the same period of 2 weeks.

Our observations in an elderly man whose quinidine clearance was enhanced by the antituberculous drug, rifampicin (Ahmad *et al.*, 1979), has led us to question this conclusion. A study by Cusack and his colleagues (1980) suggests that theophylline clearance is increased by cigarette smoking in older patients as well as younger subjects. Other investigators have reported enhancement of the metabolism of quinidine and theophylline by phenytoin in patients aged 65 years (Urbano, 1983; Kroboth *et al.*, 1983). Since phenytoin and rifampicin appear to be more powerful enzyme inducing