Bioavailability of Prednisolone Tablets

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Two four-treatment crossover studies were performed using 12 adult male volunteers in each with seven different commercially available prednisolone tablets. Plasma samples were assayed for prednisolone by a radioimmunoassay method. Statistical analyses of the data, by analysis of variance for crossover design (ANOVA), showed no significant differences among the treatment averages at any of the sampling times except at 0.25 and 4 hr in one of the studies. There were also no significant differences among the treatment averages for peak plasma level, time of peak plasma level, area 0–12 hr, area 0–24 hr, and the half-life of elimination of prednisolone. We conclude that the average plasma concentrations of prednisolone are superimposable in a statistical sense and that the tablets tested are bioequivalent. Results of dissolution studies of six tablets of each of the seven lots of prednisolone tablets, using deaerated water in the spin filter apparatus, are presented.

KEY WORDS: prednisolone bioavailability; prednisolone radioimmunoassay; prednisolone plasma concentrations; elimination half-life of prednisolone; in vitro rate of dissolution of prednisolone from tablets.

INTRODUCTION

Prednisolone, 11β,17,21-trihydroxypregna-1,4-dien-3,20-dione, is a potent corticosteroid that is offered for the palliative treatment of rheumatoid arthritis and various other diseases. Partly because of the low solubility of the drug (1), the Ad Hoc Committee on Drug Product Selection...
of the Academy of General Practice of Pharmacy included prednisolone in a list of drugs susceptible to bioavailability problems (2). Since then very few studies have appeared in the literature reporting the biological availability of prednisolone; most of these were recently reviewed in a monograph on prednisolone (3). The reviewers noted that with the exception of one study (4) all studies suffer from a number of serious experimental defects. The investigators, in these reports either have used high doses of prednisolone and failed to follow plasma levels of the drug for more than two half-lives with an insensitive colorimetric assay method (5), or have used a nonspecific assay and also failed to use the recommended crossover experimental design (6), or have studied sustained release of enteric-coated preparations (7–10). In view of the limited information on the in vivo availability of the corticosteroid following the administration of single, low doses of prednisolone in the form of compressed tablets, the studies to be reported were done. This article reports the results of two four-treatment crossover studies utilizing seven different, commercially available tablets of prednisolone.

EXPERIMENTAL

Test Products

The prednisolone tablets studied were obtained from the open market by the Food and Drug Administration, who reported to the authors that the tablets had the following average percentage of declared potency (SD in parentheses): Mc, 98.6 (3.12); St, 103.2 (2.33); Re, 98.3 (2.51); U, 98.9 (1.21); R, 105.7 (3.91); ST, 99.0 (3.00); O, 94.3 (2.50). The code letter(s) are the first one or two letters of the names of the manufacturers, and lot numbers are given in the footnote to Table I.

In Vitro Studies

The spin filter apparatus of Shah et al. (12) was used to perform in vitro dissolution rate studies. All the studies were performed at 37°C, using 1 liter of deaerated water as the dissolution medium. The dissolution studies on the same tablets are being repeated in 0.1 N hydrochloric acid using gold-plated equipment, but these results will be reported in a separate communication. The stirrer speed was maintained at 400 rpm for a period of 30 min and then it was changed to 800 rpm until a constant absorbance reading was attained. The constant absorbance value could be interpreted as the percentage of label dissolved in infinite time. Since ultraviolet-absorbing material in the tablet, other than prednisolone, may contribute to the percentage of labeled amount of prednisolone dissolved and/or the prednisolone in the