tained in intravenous and oral studies are indispensable for this purpose. Differences in the ratio of free to glucuronide-conjugated 6-desmethylgriseofulvin observed after different oral formulations (2) appear to be indicative of nonlinear kinetics for these metabolites.

The fact that highly significant statistical correlations apparently exist between 24- and 96-hr urinary metabolite excretions of a given formulation does not prove that 24-hr urinary metabolite excretion data are accurate and adequate for bioavailability assessments of griseofulvin. The existence of these correlations indicates only that a formulation with higher bioavailability will tend to give higher urinary metabolite levels at 24 and 96 hr than a formulation with lower bioavailability at these times.

Notwithstanding an apparent correlation, the bias in estimating relative bioavailabilities of different formulations using 24- rather than 96-hr urinary excretion total metabolite data can be demonstrated with the data reported by Bates and Sequeira (2). They investigated the cumulative urinary excretion of total 6-desmethylgriseofulvin after the administration of four different griseofulvin formulations to five individuals. On the assumption of first-order kinetics, the relative bioavailability of the four different griseofulvin formulations can be calculated from the ratios of the mean amounts of total metabolite excreted in urine at different times (Table I).

It is evident that the use of 24-hr urinary excretion data of total metabolite leads consistently to underestimations of derived relative bioavailabilities. The underestimation increases with the smaller bioavailabilities, consistent with the premise that delayed absorption is the primary reason for low bioavailability. Thus, underestimation will be greatest when the relative bioavailability of poorly absorbed formulations is studied[1].

The standard error of the mean, expressed as percent of the mean, was consistently larger for the total amount of urinary metabolite at 24 hr. At 24 hr, the values were: I, 11.5%; II, 18.3%; III, 15.6%; and IV, 4.6%. At 96 hr, they were: I, 5.4%; II, 12.2%; III, 10.6%; and IV, 4.2%. Thus, routine assessments of bioavailabilities of different griseofulvin formulations should not be based on 24-hr urinary excretion data of total 6-desmethylgriseofulvin even if first-order kinetics exist.

I feel strongly that this dangerous procedure of using fractional urinary excretion data and/or areas (1, 3, 4) for the assessment of bioavailability must be clearly recognized.

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[1] The rank order for the bioavailability of products in Table I is the same at 24 as it is at 96 hr (IV > III > II > I).

BOOKS

REVIEWS

Aliphatic Chemistry, Volume 3, Specialist Periodical Report. Senior Reporter, A. McKILLOP. The Chemical Society, Burlington House, London WIV OBN, England, 1975. xii + 409 pp. 14.5 × 22 cm. Price £13.50.

The first volume of "Aliphatic Chemistry" was published as Part I of a three-part Specialist Periodical Report on aliphatic, alicyclic, and saturated heterocyclic chemistry. Subsequently, these areas have been reviewed in separate Specialist Periodical Reports. This Specialist Report is the third volume of the series, dealing with aliphatic chemistry and, except for one chapter, reviews the literature published during 1973. Chapter 1, by R. S. Atkinson, is devoted to acetylenes, alkanes, allenes, and alkenes; Chapter 2, by E. W. Colvin, surveys the literature on other functional groups (carboxylic acids, esters, lactones, anhydrides, amides, nitriles, aldehydes and ketones, alcohols, amines, alkyl halides, ethers, and sulfur compounds). These chapters are similar in format and style to analogous chapters by the same authors in the two preceding volumes.

This volume, like Volume 2, contains chapters that summarize progress in the area of naturally occurring polyolefinic and polyacetylenic compounds (Chapter 3) and in the chemistry of the prostaglandins (Chapter 4). Both chapters are authored by G. Pattenden, as were the corresponding chapters in Volume 2. The literature on fatty acids and related compounds was reviewed in Volume 1 but not in Volume 2. Developments in this area during both 1972 and 1973, therefore, comprise Chapter 5 by F. D. Gunstone. The specialized areas of Chapters 3–5 are exemplified by sections dealing with polyolefinic antibiotics and other microbial metabolites, insect pheromones, acetylenes and olefins of marine or plant origin, prostaglandin syntheses, the multifaceted aspects of studies of fatty acids, and others.

A cumulative set of volumes may serve as summaries of the literature for the specialist engaged in research in one of these areas; but, perhaps more importantly, these annual surveys will provide a means by which others may be introduced to, or become familiar with, developments in a specific area. The value of surveys of the annual literature devoted to specific areas, such as those of Chapters 3–5, is readily recognized. Reviews of the more general topics of the first two chapters are equally valuable, since much effort would be required for the individual to extract this type of information from the periodical or abstract literature. In giving comprehensive coverage of the significant literature, the authors maintain the high standards of the preceding volumes.

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