ABSORPTION, PROTEIN BINDING, AND ELIMINATION OF RIBOFLAVIN

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The absorption, distribution, metabolism, and excretion of riboflavin have been studied most extensively in man and in the rat. These studies have revealed considerable species differences in the intestinal absorption, protein binding, biliary excretion, and renal excretion of the vitamin. Fortunately, the pharmacologic innocuousness and the availability of good methods for the quantitative analysis of riboflavin in biological fluids and tissues have permitted detailed investigation of the pharmacokinetic characteristics of the vitamin in man. Most of these studies have been carried out with relatively large doses of riboflavin (>0.1 mg/kg), considerably in excess of the amounts that satisfy nutritional requirements. Such studies are therefore useful more for elucidating mechanisms of absorption and elimination of the vitamin, rather than for illustrating the quantitative aspects of these processes when riboflavin is derived entirely from normal dietary sources.
1. ABSORPTION

1.1. Normal Patterns of Riboflavin Absorption

Considerable differences in absorption and disposition of riboflavin among species have led to confusion concerning the degree and mechanism of intestinal absorption of riboflavin. In man, riboflavin is absorbed to an appreciable degree by a specialized transport process that appears to be localized in the proximal small intestine. Evidence for this, to be described in greater detail in subsequent paragraphs, takes the following nature:

1. Site specificity of intestinal absorption is shown by the absorption of as much as 60% of an oral dose of riboflavin, while similar doses administered rectally yield only about 10% absorption.
2. Studies of the absorption of riboflavin administered in various pharmaceutical dosage forms have shown that the vitamin must be released promptly (i.e., in the proximal region of the intestinal tract) from the product, or absorption will be diminished.
3. Saturability of intestinal absorption of riboflavin has been demonstrated by the administration of 5- to 300-mg doses of the vitamin of which decreasing fractions are recovered in the urine as the dose is increased.
4. Specialized transport is also indicated by the fact that riboflavin absorption from oral doses can occur at an extremely rapid rate, while the physicochemical properties of the vitamin suggest that passive diffusion across the intestine should be slow.

1.1.1. Intestinal Absorption in Man

The absorption of riboflavin and FMN has usually been studied in man by following the urinary excretion of the vitamin. This method of elucidating the absorption characteristics of the vitamin in man is valid as long as: (a) large doses (>5 mg) are used, (b) comparison is made of data obtained after oral and parenteral doses, (c) the time course of excretion is followed until no further elimination of the dose occurs (8-24 hr), and (d) concentration-dependent effects on the renal clearance of riboflavin are recognized as a confounding factor. (These precautions apply as well to the examination of plasma concentration data.) The application of pharmacokinetic principles is helpful because they sort out the simultaneously acting variables and because plasma