vitamin E. Twelve subjects were studied by chemical balance techniques when taking 200mg. of vitamin E acetate orally/day.

Urine radioactivity never exceeded 6% and will not be discussed further.

The overall absorption in group A varied from 61% to 90% (mean 75%) and in group B from 31% to 84% (mean 61%). The difference between the two groups was significant ($P < 0.001$). There was a significant correlation between the amount absorbed and the degree of steatorrhoea expressed as g. of fat/day ($P < 0.001$). Greater than 70% of the faecal activity was present as unchanged α -tocopherol and excreted over the first three days; thereafter less than 1%/day was excreted.

The plasma radioactivity curves were significantly different for the two groups but there was an overlap; the peak of radioactivity for both groups was at 8 hr. Erythrocyte radioactivity curves paralleled the corresponding plasma curves but the amount of radioactivity was only approximately 10% of the plasma concentration.

Repletion with the vitamin did not alter its absorption.

Absorption is dose-dependent, as judged by comparison with therapeutic doses of vitamin E (200mg./day) in some of the same subjects.

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The Absorption and Distribution of Tocochromanols in the Rat

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The eight naturally occurring tocochromanols fall into two series, α -, β -, γ - and δ -tocopherol and the related compounds, α -, β -, γ - and δ -tocotrienol, differing only in having three double bonds in the isoprenoid side-chain. α -Tocopherol has been shown to have the greatest biological potency of the compounds so far studied; the order of potency is α -tocopherol > β -tocopherol > α -tocotrienol > γ -tocopherol > β -tocotrienol > δ -tocopherol (Bunyan, McHale, Green & Marcinkiewicz, 1961). The order of biological potency of the tocopherols is reflected in the tissue concentrations after oral dosing (e.g. Griffiths, 1959). The absorption and distribution of all the naturally occurring tocochromanols has been studied to compare tissue concentrations further with biological potency, more especially for α - and β -tocotrienol, and to

study the differences in uptake brought about by the small changes in chemical structure.

Groups of female albino rats were given a dose of 12–20mg. of tocochromanol. The rats were killed 2, 4, 8, 16 or 24 hr. after dosing, and the small intestine, liver, spleen, heart, kidney, skeletal muscle and brain were removed. Tocochromanols were isolated from the tissues and estimated by the method of Emmerie & Engel (1938).

Maximum concentrations of tocochromanol were found in the liver 4 hr. after administration and the concentration declined continuously thereafter. The relative order of uptake in the liver, based on tissue concentrations 4 hr. after dosing, was α -tocopherol (8.9% of the dose) > α -tocotrienol (7.6%) > β -tocopherol (6.4%) > γ -tocopherol (2.3%) > δ -tocopherol (1.6%) > β -tocotrienol (1.5%) > γ -tocotrienol (0.7%) > δ -tocotrienol (0.3%). Each tocopherol was absorbed more effectively than the corresponding tocotrienol. The relative order of uptake in both series of compounds was α -(5,7,8-trimethyl) > β -(5,8-dimethyl) > γ -(7,8-dimethyl) > δ -(8-methyl). The effect of three double bonds in the side chain was to decrease considerably the maximum concentration found in the liver and to increase the rate of decline from the maximum. This order of uptake was not the same in all tissues. In heart, muscle and kidney, the tocotrienols were found in amounts equal to or greater than those of the corresponding tocopherols. No tocotrienol was detected in the spleen after 8 hr. after dosing; the tocopherols were detectable after 24 hr. No tocochromanol was found in the brain over the 24 hr. period. The pattern of maximum uptake shows α -tocotrienol to be absorbed more efficiently than β -tocopherol, although its biological potency is less, whereas β -tocotrienol is absorbed less efficiently than δ -tocopherol, although its biological potency is probably greater. The results demonstrate considerable variation in ratio between tissue concentrations at different times after dosing. For example, the ratio of α -tocopherol to α -tocotrienol in the liver was 100:85 4 hr. after dosing, but 24 hr. after dosing the ratio was 100:7, the tocopherol being more effectively retained. Suggested ratios for biological potency derived from tissue-storage tests therefore depend very much on the time-interval between final dosing and subsequent tissue analysis.

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