

Uptake, Secretion and Metabolism of Vitamin E by Differentiated Caco-2 Monolayers in Transwell Culture

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Nathalie Nicod, Cornell University, Ithaca (previously Lausanne, CH)

Vitamin E is a family of eight different vitamers, four tocopherols (TOH) and four tocotrienols, which have very similar structures but are retained very differently in plasma and in tissues. The body discriminates among them by retaining one vitamer, α -Tocopherol, (α -TOH) and metabolizing the others. It is known that the liver plays a role in this discrimination, however it is unclear if the intestine exhibits any selectivity in the absorption of the different vitamers. Selectivity could be accomplished by differential uptake into enterocytes, metabolism within enterocytes, or/and secretion from enterocytes. We hypothesize that enterocytes of the small intestine discriminate in favor of α -tocopherol by mechanisms operative at tocopherol dosages typical of meals.

The Caco-2 cell line is a colon adenocarcinoma cell line, which is considered the model of choice in investigating processes of intestinal absorption. Therefore these cells are of potential value in studying the selective uptake, secretion and metabolism of the different Vitamin E vitamers. Our laboratory has determined that Caco-2 cells differentially metabolize tocopherols by the same mechanism and in the same order as in liver (δ -TOH > γ -TOH > α -TOH). Caco-2 cells once confluent differentiate and polarize forming an apical membrane, which corresponds to the membrane exposed to the lumen, and a basolateral membrane, which corresponds to the membrane in contact with plasma. By growing Caco-2 cells on transwells it is possible to add vitamin E apically in bile salt micelles and measure uptake as well as secretion from the basolateral membrane. We have determined that the uptake of Vitamin E by Caco-2 cells is concentration dependent as well as vitamer specific. At low concentrations (10 μ M) α -, γ - and δ -TOH are taken up equally. However, at higher concentrations (50 μ M) δ -TOH is taken up more efficiently by Caco-2 cells and α -TOH is the least well taken up (δ -TOH > γ -TOH > α -TOH). Basolateral secretion is also concentration dependent and vitamer specific. At low concentrations basolateral secretions of α -, γ - and δ -TOH are equivalent. However, at higher concentrations δ -TOH secretion is greater than α -TOH (δ -TOH > γ -TOH > α -TOH). Secretion efficiencies, the percent of vitamer secreted relative the amount of vitamer taken up by the cells, are equivalent for all three vitamers at low concentrations. However, when the vitamers are administered at higher concentration the order of secretion efficiency is α -TOH > γ -TOH > δ -TOH.

These results indicate that the differentiated Caco-2 monolayer/transwell model is a useful tool for studying uptake and secretion of tocopherols, and current work is focusing on the mechanisms involved.