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Changes in Isoprenoid Lipid Synthesis by Gemfibrozil and Clofibric Acid in Rat Hepatocytes

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We studied whether gemfibrozil and clofibric acid alter isoprenoid lipid synthesis in rat hepatocytes. After incubation of the cells with the agent for 74 hr, [^{14}C]acetate or [^{3}H]mevalonate was added, and the cells were further incubated for 4 hr. Gemfibrozil and clofibric acid increased ubiquinone synthesis from [^{14}C]acetate and [^{3}H]mevalonate. The effect of gemfibrozil was greater than that of clofibric acid. Also, gemfibrozil decreased dolichol synthesis from [^{14}C]acetate and [^{3}H]mevalonate. However, clofibric acid increased dolichol synthesis from [^{3}H]mevalonate. Gemfibrozil decreased cholesterol synthesis from [^{14}C]acetate and [^{3}H]mevalonate. Clofibric acid decreased cholesterol synthesis from [^{14}C]acetate, but did not affect synthesis from [^{3}H]mevalonate. These results suggest that both agents activate the synthetic pathway of ubiquinone, at least from mavalonate. Gemfibrozil may inhibit the synthetic pathway of dolichol, at least from mevalonate. Contrary to gemfibrozil, clofibric acid may activate the synthetic pathway of dolichol from mevalonate. Gemfibrozil may inhibit the synthetic pathway of cholesterol from mevalonate in addition to the pathway from acetate to mevalonate inhibited by both agents.