METABOLISM OF DRUGS BY HUMAN INTESTINAL MICROFLORA

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Gastrointestinal tract includes millions of bacteria that in principle can metabolize orally administered drugs. The main aim of our study was to find out whether selected drugs with various chemical structures can be metabolized by bacteria present in human intestine. Tenofovir, drug used to prevent and treat HIV/AIDS and hepatitis B, diazepam, sedative and anxiolytic drug, and nabumetone, nonsteroidal anti-inflammatory drug, were incubated with fresh human intestinal bacteria. 1 g of human stool was mixed in Mueller-Hinton broth and left for 2 h at 35°C. After 2 hours, solutions of selected drugs were added into the inoculated broth. The incubation of broth with drugs took 6 h or 20 h at 37°C. Subsequently, the reaction was stopped by cooling down to 4 °C and by precipitation of proteins by mixture of methanol, acetonitrile, and water (4:5:1, v/v). Supernatants were injected into LC/MS. Control samples (broth alone or with drugs without bacteria, inoculated broth without bacteria and drugs) were prepared in the same way. Results show that compounds are metabolized in different ways. One hydrogenated metabolite was found in samples with nabumetone. Two metabolites (formed by decomposition and/or demethylation) were detected in samples with diazepam. Samples with tenofovir contained four different metabolites. Reactions that participated in tenofovir metabolism were demethylation, hydroxylation, and hydrogenation. The results show that the bacteria of human gut microbiome can be involved in drug biotransformation in human gastrointestinal tract.

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