Drug Metabolism by Fungi Colonizing Decomposing Human Cadavers

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Even during lifetime, the human body is colonized by a microflora which primarily consists of bacteria native to the gastrointestinal tract but also includes some fungi that are generally located in various areas of the skin, genitourinary, and gastrointestinal tract. After death, these microbes may colonize the entire corpse which provides a good nutritive medium for microorganisms, especially in advanced stages of decomposition. This colonization could be relevant to case interpretation in postmortem toxicology, because microbiological degradation of drugs and poisons could affect the concentrations and/or metabolic profiles of these compounds in postmortem specimens. However, knowledge on postmortem microbial drug metabolism is limited to a few reports e.g. on hydrolysis of glucuronides of ethanol and morphine, the reduction of nitrobenzodiazepines to their amino metabolites, or reductive cleavage of the isoxazol moiety of risperidone and its 9-hydroxy metabolite. All of these reactions are catalyzed by bacteria. In contrast, postmortem microbial metabolism by fungi has been largely ignored until recently.

In this presentation, the results of the studies on drug metabolism by fungi colonizing cadavers performed by the author's research group will be summarized and discussed. Fungi were retrospectively and prospectively isolated from various postmortem materials collected during autopsy of decomposed human bodies (heart blood, liver, kidney, and lung). Identification of the isolates was achieved morphologically by microscopy and molecularly by polymerase chain reaction (PCR), amplification, and sequencing of markers allowing species identification of the respective genera. A total of 156 fungal strains could be isolated and characterized. They belonged to 28 species from 15 genera, of which Candida was the most frequent followed by Penicillium, Rhodotorula, Mucor, Aspergillus, Trichosporon, and Geotrichum. Twenty eight of the fungal strains (one per species) were tested for their in vitro metabolic capacity towards the model drugs amitriptyline, metoprolol, mirtazapine, promethazine and zolpidem. Cultures of each fungal strain were incubated with each of the model drugs and the fungus Cunninghamella ellegans was used as positive control. Aliquots of the incubation mixture were analyzed by LC-ESI-MS/MS with product ion scanning and by full scan GC-MS. All the tested fungal strains were capable of forming mammalian phase I metabolites, but the number of metabolites and extent of biotransformation differed considerably between strains. Some of the metabolites formed by the fungi have not been described in mammals. Initial experiments with authentic postmortem case samples suggest that these might serve as marker compounds for postmortem fungal metabolism.

In conclusion, it can be stated that fungi can colonize decomposing human bodies and that they are capable of catalyzing metabolic phase I reactions similar to those occurring in humans. It therefore seems likely that fungi colonizing cadavers can change the concentrations and metabolite patterns in postmortem samples, although the extent and relevance of these changes is yet unclear.