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LETTER TO THE EDITOR, NEWS AND VIEWS

Future study for the urinary histidine adduct derived from pyrrolizidine alkaloids is warranted

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We received comments from a reader on our recently published research article entitled "Developing urinary pyrrole-amino acid adducts as non-invasive biomarkers for identifying pyrrolizidine alkaloids–induced liver injury in human (https://doi.org/10.1007/s00204-021-03129-6)". In this study, we detected pyrrole-9-histidine in urine of rats and patients exposed to pyrrolizidine alkaloids and identified the structure by comparison of its HPLC retention time and mass spectrum with those of a synthetic standard with the pyrrole moiety attached to the histidine *N*-terminal. However, since this urinary pyrrole-9-histidine is likely formed from degradation of pyrrole-protein adducts in the body, this reader suggested that based on protein biochemistry, the structure of pyrrole-9-histidine that we identified in the urine should be favorably the one with the pyrrole moiety attached to the N atom in the imidazole of histidine. We agree with this reader's suggestion. According to the experimental results obtained so far, we cannot unequivocally determine the structure of this urinary pyrrole-9-histidine, although the pyrrole-9-histidine isomer with its pyrrole moiety attached to the imidazole is favorable to the N-terminal of histidine isomer. Future study is warranted to identify the structure of this urinary pyrrole-9-histidine.

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