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Biliatresone, a novel toxin of *Dysphania* species, spontaneously conjugates with glutathione and amino acids

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Localized outbreaks of biliary atresia (BA) in newborn animals have been reported three times in Australian livestock. These years had in common (i) severe drought, (ii) the animals in pregnant dams were grazed on lands normally under water, and (iii) the flora of these pastures consisted of large relative abundances of *Dysphania glomulifera* and *D. littoralis*. To identify the toxic constituent of BA, we collected the plants grown at the place of the 2007 outbreak. As an animal model of BA in vivo, we used the zebrafish biliary bioassay system. Through the bioassay-guided sequential separation, we isolated betavulgarin derivative, biliatresone, with a yield of 1.84% of the dry weight. Biliatresone is a novel isoflavone metabolite with a strong electrophilic exocyclic enone. The extrahepatic biliary system of biliatresone-treated zebrafish showed morphological defects of the gallbladder at a concentration of 0.125 µg/mL as well as of the extrahepatic bile ducts at a higher concentration of 1.0 µg/mL. Biliatresone was isolated by RP-HPLC together with a water conjugate and a methanol conjugate, indicating a spontaneous conjugation with mobile solvents used in the HPLC. Biliatresone also spontaneously conjugates with glutathione (GSH) and several amino acids (cysteine, histidine, glycine, glutamate, and phenylalanine) suggesting a potential mechanism for cellular and systemic toxicities. These results demonstrate that biliatresone is a plant toxin which has the strong electrophilic capability that might attack the animal biliary system.

Biography

Kyung A Koo has completed her PhD from Seoul National University, South Korea and postdoctoral studies from Seoul National University, College of Pharmacy. She is currently the research associate of University of the Sciences in Philadelphia, USA. She has published more than 25 papers in peer-reviewed journals.

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