

B-11**Metabolism and Disposition of Antrodin C in Rats: Extreme Hepatic Transformation and Biliary Excretion**

左 風¹、和田明穂¹、○馬 超美¹、中村憲夫²、服部征雄¹
¹富山大学 和漢医薬学総合研究所 薬物代謝工学分野、²同志社女子大学薬学部化学系生薬学研究室

Antrodin C (3-isobutyl-4-[4-(3-methyl-2-butenyloxy)phenyl]-1H-pyrrole-2,5-dione) was isolated from the mycelium of *Antrodia camphorata*, which possessed potential cytotoxic and hepatoprotective effects. The metabolites of antrodin C in rats were identified using liquid chromatography/electrospray ionization/ion trap mass spectrometry. The metabolites in the feces samples were (2Z)-2-isobutyl-3-{4-[(3-methylbut-2-en-1-yl)oxy]phenyl}but-2-enedioic acid (M1), (2Z)-2-isobutyl-3-{4-[(3-methylbut-2-en-1-yl)oxy]phenyl}but-2-enedioic acid 4-methyl ester (M2), (2Z)-2-isobutyl-3-{4-[(3-methylbut-2-en-1-yl)oxy]phenyl}but-2-enedioic acid 1-methyl ester (M3) and antrodin B (M5); the metabolites in the bile were M2, M3 and antrodin A (M4). Incubation with intestinal bacterial mixture, the metabolites (M2-4) in the bile samples were thoroughly converted to M1 after 30 min. Therefore, it suggested that antrodin C was metabolized to M2-4 in the liver and excreted by bile, and then M2-M4 were transformed to M1 by intestinal bacteria in large intestine, which was again absorbed into blood. Subsequently, pharmacokinetics of M1 was analyzed in the bile duct-cannulated (BDC) rats after oral administration of antrodin C (50 mg/kg) and intravenous injection (10 mg/ml) by PAD-HPLC. After oral administration, $t_{1/2(k\alpha)}$ and $t_{1/2(k\beta)}$ were 0.95 h and 12.64 h, respectively. AUC_{0-12h} were 1.61 (P.O.) and 1.68 h mg/ml (I.V.), $Cl_m.b.$ was 5.96 ml/h kg and $F_m.b.$ was 19.43 (%). Antrodin C was quickly absorbed from gastrointestinal tract and metabolized in the liver, the main excretion was bile-feces pathway in rats.

B-12 ★**Constituents of *Boesenbergia pandurata* and Their cytotoxicity against PANC-1 Cells under Nutrient Deprived Condition**

○NWET WIN NWET¹, Awale Suresh¹, Esumi Hiroyasu², Tezuka Yasuhiro¹, Kadota Shigetoshi¹

¹Division of Natural Products Chemistry, Institute of Natural Medicine, University of Toyama, ²Investigative Treatment Division, National Cancer Center Research Institute East

Pancreatic cancer is an aggressive disease with the lowest 5-year survival rate of all cancers. It is largely resistant to conventional forms of treatment and the development of more effective treatment is urgently needed. Among different forms of cancer, pancreatic cancer cells have remarkable tolerance against extreme nutrient starvation enabling them to survive for prolonged period of time even in critically low nutrient condition. Thus, the elimination of this tolerance of cancer cells to nutrient starvation might be a new biochemical approach in cancer therapy. Under this approach, a new screening strategy has been developed for the discovery of anticancer agents that preferentially eliminates the tumor cells capability to survive under low nutrition condition using PANC-1 cancer cell line, termed as anti-austerity strategy. Under this strategy, screening of medicinal plants from Myanmar was carried out and found that the chloroform extract of *Boesenbergia pandurata* exhibited 100% preferential cytotoxicity at a concentration of 10 μ g/mL. Thus, detailed phytochemical investigation was carried out, which yielded four new compounds, geranyl-2,4-dihydroxy-6-phenethylbenzoate (1), 2',4'-dihydroxy-3'-(1"-geranyl)-6'-methoxychalcone (2), 2-hydroxyisopanduratin A (3), and 8-geranylpinostrobin (4) along with twenty known compounds (5-24). Among the known compounds, 6-geranylpinostrobin (5), 6-methoxyisopanduratin A (6), and 7,8-dihydro-5-hydroxy-2-methyl-2-(4"-methyl-3"-pentenyl)-8-phenyl-2H,6H-benzo[1,2-b:5,4-b']dipyran-6-one (7) were isolated for the first time from the natural source. The isolated compounds showed varying degrees of an in vitro preferential cytotoxicity. Among them, Panduratin A (15) and nicolaioidesin B (17) exhibited the most potent preferential cytotoxicity at 2.5 μ M.