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Metabolism and Disposition of Antrodin C in Rats: Extreme Hepatic Transformation and Biliary Excretion

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Antrodin C (3-isobutyl-4-[4-(3-methyl-2-butenyloxy)phenyl]-1H-pyrrole- 2,5-dione) was isolated from the mycelium of Antrodia camphorate, 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-methy ester (M3) and antrodin B (M5); the metabolites in the bile wre 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. $AUC_{0\text{-}lim}$ were 1.61 (P.O.) and 1.68 h mg/ml (I.V.), Clm.b. was 5.96 ml/h kg and Fm.b. was 19.43 (%). Antrodin C was quickly absorbed from gastrointestine and metabolized in the liver, the main excretion was bile-feces pathway in rats.

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

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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 μg/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-methoxypanduratin A (**6**), and 7,8-dihydro-5-hydroxy-2-methyl-2-(4''-methyl-3''-pentenyl)-8-phenyl-2*H*,6*H*-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 μM.