Evaluation water solubility and *in vitro* biotransformation of four YC-1 prodrugs

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Benzyl-3-(5-hydroxymethyl-2-furyl) indazole (**YC-1**) has a variety of pharmacological activities and distinct mechanisms, but its water solubility as well as oral absorption rate is poor. To improve its water solubility, four hydrophilic prodrugs **YC-M1**, **YC-1-G**, **YC-1-S** and **119-2** were designed, synthesized and evaluated their water solubility and bio-transformation in simulated intestinal fluid and liver microsome.

Four derivatives (0.25 mg each) were respectively added to fresh prepared simulated intestinal fluid (250 μl) for 15 min, 30 min, 1 h and 2 h and then ethyl acetate(EA) (250 μl) was used to extract the product. After EA evaporated, the residue was reconstituted with methanol (200 μl) and analyzed by HPLC. The result showed no significant metabolic effects was found in **YC-1**(retention time (RT): 5.3~5.4 min), **YC-M1** (RT: 5.9 min) and compound **119-2** (RT: 4.8 min) after 2 h. However, the peak of **YC-1-G** (RT: 2.7~2.8 min) was gradually transformed into two peaks (RT: 3.6 min and 4.8 min) after 15 min. The peak of another hydrophilic **YC-1-S** (RT: 6 min) after 15 min showed obvious reduction which implied strong metabolic effect occurred. Further structure identification of the metabolites still needs to be addressed.

These results showed **YC-1-G** and **YC-1-S** have great development potential and merit further discussion.