



Assessment of Effects of Chidamide on CYP450 Isoforms Activity of Rats by Cocktail Approach

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SUMMARY. Chidamide is a new histone deacetylase (HDAC) inhibitor of the benzamide class currently under clinical development in cancer indications. Cocktail method was used to evaluate the influence of chidamide on the activities of CYP450 isoforms CYP2B6, CYP2D6, CYP3A4, CYP2C19, and CYP2C9, which were reflected by the changes of pharmacokinetic parameters of 5 specific probe drugs bupropion, metoprolol, midazolam, omeprazole, and tolbutamide, respectively. The experimental rats were randomly divided into two groups, control group and chidamide group. The chidamide group rats were given 15 mg/kg by oral administration once a day for 7 days. The mixture of 5 probes was given to rats through oral administration and the blood samples were obtained at a series of time-points through the caudal vein. The concentrations of probe drugs in rat plasma were measured by liquid chromatography-tandem mass spectrometry (LC-MS). In the experiment for chidamide and control group, there was no statistical pharmacokinetic differences for bupropion, midazolam, and omeprazole, while there was statistical pharmacokinetic differences for metoprolol and tolbutamide. Chidamide could not influence the activities of CYP450 isoforms CYP2B6, CYP2D6, CYP3A4, CYP2C19, and CYP2C9 of rats, while it could inhibit the activities of CYP2D6 and CYP2C9.

KEY WORDS: CYP450, Chidamide, Cocktail, LC-MS.

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