

**Serum drug exposure of COMPOUND 3 in WO 2023/040937 A1 and
COMPOUND of Example 65 in WO 2009/127546 A1**

(1) Methods

Testing compounds (COMPOUND 3 and COMPOUND Example 65) were prepared in a formulation of 0.5% HPC plus 0.1% Tween 80 suspension (3 mg/mL).

Wild type (WT) mice were fasted for 2 hours, then received COMPOUND 3, or COMPOUND Example 65 at a dose of 30 mg/kg via oral gavage. Mice serum was collected at 1 hour post drug administration for drug exposure determination, including concentrations of testing compounds and concentration of the active metabolites HMS5552 (parent drug) by using LC-MS/MS (Triple Quad 6500 plus).

(2) Results

(2.1) Serum drug exposure

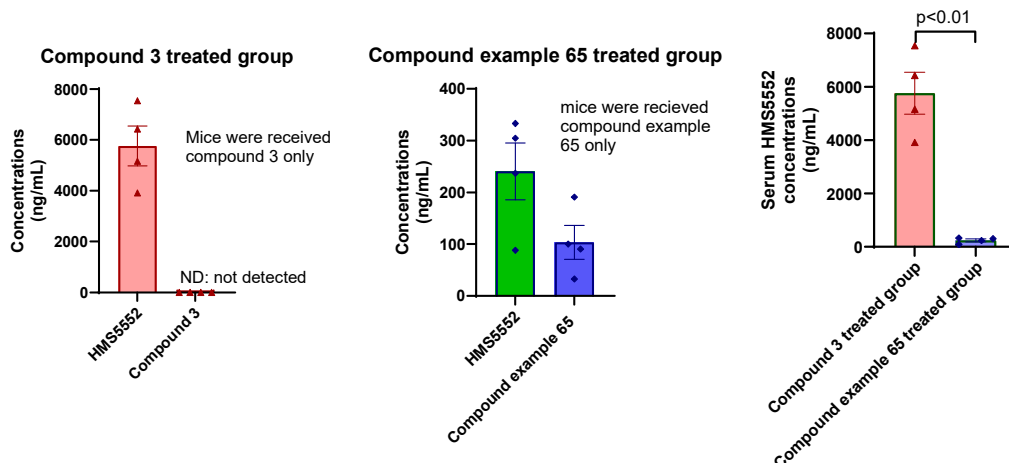


Figure 1

Figure 2

Figure 3

Figure 1: Concentrations of COMPOUND 3 and HMS5552 in serum in COMPOUND 3 treated group.

Figure 2: Concentrations of COMPOUND Example 65 and HMS5552 in serum in COMPOUND Example 65 treated group.

Figure 3: Comparison of serum HMS5552 concentrations in COMPOUND 3 treated group and COMPOUND Example 65 treated group.

As shown in Figure 1, only HMS5552 was detected in COMPOUND 3 treated group, COMPOUND 3 itself was undetectable (the limit of quantification is 1 ng/mL), suggesting that COMPOUND 3 was completely converted to HMS5552 in WT mice.

As shown in Figure 2, both COMPOUND Example 65 and HMS5552 were detected in

Exhibit 1

COMPOUND Example 65 treated group, suggesting that only a fraction of COMPOUND Example 65 was converted to HMS5552.

As shown in Figure 3, comparison of serum concentrations of HMS5552 in COMPOUND 3 treated group and in COMPOUND Example 65 treated group shows that serum concentration of HMS5552 in COMPOUND 3 treated group was much more than that in COMPOUND Example 65 treated group ($P < 0.01$).