**Supporting information**

Development and in vitro−in vivo correlation evaluation of IMM-H014 extended–release tablets for the treatment of fatty liver disease

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# Table S1. Saturated solubility of IMM-H014 in different media

|  |  |
| --- | --- |
| **pH** | **Saturation solubility (mg/mL)** |
| 2.0 | 229.1 |
| 4.5 | 32.5 |
| 6.8 | 5.0 |
| 12.0 | 0.0 |

#  Table S2 Cumulative percentage drug release of IMM-H014 tablet with different matrix materials (F1 to F4)

|  |  |
| --- | --- |
| **Time (h)** | **IMM-H014（%）** |
| **F1** | **F2** | **F3** | **F4** |
| 0.5 | 3.4 | 1.4 | 6.1 | 11.9 |
| 1 | 7.3 | 2.3 | 12.0 | 19.7 |
| 2 | 14.8 | 4.5 | 22.2 | 29.0 |
| 3 | 22.1 | 7.1 | 30.0 | 36.1 |
| 4 | 29.1 | 9.7 | 36.8 | 41.6 |
| 6 | 41.8 | 14.3 | 49.0 | 50.2 |
| 8 | 54.5 | 18.8 | 60.7 | 57.8 |
| 10 | 65.4 | 22.7 | 69.7 | 64.1 |
| 12 | 74.8 | 26.3 | 76.9 | 69.4 |
| 16 | 86.7 | 32.5 | 85.8 | 78.0 |
| 20 | 93.9 | 37.6 | 89.1 | 84.8 |
| 24 | 96.4 | 42.1 | 90.1 | 89.6 |

# Figure S1. In vitro release profiles of tablet with different matrix materials (F1 to F4) in 0.01N HCl →pH 7.5 PBS medium

**Table S3** Cumulative percentage drug release of IMM-H014 tablet with HPMC concentration (IR, F5 to F10)

|  |  |
| --- | --- |
| **Time (h)** | **IMM-H014（%）** |
| **IR** | **F5** | **F6** | **F7** | **F8** | **F9** | **F10** |
| 0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 0.08 | 62.3 | / | / | / | / | / | / |
| 0.17 | 91.0 | / | / | / | / | / | / |
| 0.25 | 95.0 | / | / | / | / | / | / |
| 0.33 | 96.4 | / | / | / | / | / | / |
| 0.5 | 97.6 | 10.2 | 12.6 | 13.2 | 13.9 | 32.8 | 46.4 |
| 0.75 | 98.5 | / | / | / | / | / | / |
| 1 | 99.5 | 18.6 | 20.7 | 23.8 | 23.9 | 49.6 | 71.9 |
| 1.5 | 99.6 | / | / | / | / | / | / |
| 2 | 99.7 | 29.1 | 33.1 | 39.2 | 39.0 | 72.5 | 99.6 |
| 3 | 99.7 | 32.4 | 34.7 | 40.7 | 43.2 | 73.3 | 95.1 |
| 4 | 99.8 | 33.4 | 37.7 | 44.3 | 48.5 | 79.6 | 97.1 |
| 6 | 99.8 | 37.1 | 44.0 | 51.6 | 57.5 | 88.2 | 97.6 |
| 8 | / | 41.4 | 51.3 | 59.7 | 64.0 | 91.3 | 97.8 |
| 10 | / | 46.1 | 58.9 | 67.5 | 72.6 | 94.3 | 98.3 |
| 12 | / | 51.1 | 66.0 | 74.5 | 80.3 | 95.5 | 98.4 |
| 16 | / | 61.0 | 77.5 | 84.4 | 86.2 | 96.8 | 99.1 |
| 20 | / | 69.8 | 85.7 | 91.0 | 93.0 | 96.9 | 99.2 |
| 24 | / | 77.2 | 91.1 | 95.4 | 96.9 | 97.1 | 99.4 |

# Table S4. Pharmacokinetic parameters of ER with different HPMC concentration and IR

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Pharmacokinetic parameters** | **IR** | **F5** | **F6** | **F7** | **F8** | **F9** | **F10** |
| AUC(0-t) (ng·h/m) | 11415.9 | 6691.7 | 7377.1 | 8395.1 | 9894.3 | 10980.8 | 10209.2 |
| AUC(0-∞) (ng·h/m) | 11545.2 | 7034.5 | 7904.8 | 9480.3 | 10508.1 | 11393.3 | 10579.6 |
| MRT(0-t) (h) | 4.2 | 7.255 | 7.7 | 8.095 | 6.838 | 7.201 | 6.359 |
| MRT(0-∞) (h) | 4.5 | 8.365 | 9.5 | 10.948 | 8.135 | 8.019 | 7.410 |
| Tmax (h) | 0.5 | 3.13 | 2.3 | 2.75 | 1.63 | 3.10 | 2.20 |
| Cmax (ng/mL) | 4447.8 | 739.4 | 798.1 | 781.6 | 1326.5 | 1276.8 | 1553.9 |
| F（%） | 100% | 58.6 | 64.6 | 73.5 | 86.7 | 96.2 | 89.4 |

# Table S5. Cumulative percentage drug release of IMM-H014 ER tablets in five different dissolution media

|  |  |
| --- | --- |
| **Time (h)** | **IMM-H014 (%)** |
| **0.01M HCl→pH7.5 PBS** | **0.01M HCl** | **pH4.5 PBS** | **water** | **pH4.5 PBS** |
| **IMM-H014-TB2-1** | **IMM-H014-TB2-2** | **IMM-H014-TA2-1** | **IMM-H014-TB2-1** | **IMM-H014-TB2-2** | **IMM-H014-TA2-1** | **IMM-H014-TB2-1** | **IMM-H014-TB2-2** | **IMM-H014-TA2-1** | **IMM-H014-TB2-1** | **IMM-H014-TB2-2** | **IMM-H014-TA2-1** | **IMM-H014-TB2-1** | **IMM-H014-TB2-2** | **IMM-H014-TA2-1** |
| 0 | 0 | 0 | 0 | 0.0 | 0.0 | 0.0 | 0.0  | 0.0  | 0 | 0.0 | 0.0 | 0 | 0.0  | 0.0  | 0 |
| 0.5 | 20.2 | 19.8 | 20.4 | 20.0 | 19.7 | 19.9 | 17.9  | 18.1  | 17.6  | 19.9 | 18.7 | 19.5 | 17.9  | 18.1  | 17.6  |
| 1 | 33.7 | 33.2 | 33.5 | 33.0 | 32.3 | 32.8 | 29.5  | 29.6  | 29.7  | 32.5 | 31.2 | 30.1 | 29.5  | 29.6  | 29.7  |
| 2 | 52.2 | 51.5 | 51.1 | 51.0 | 49.7 | 49.6 | 45.5  | 45.6  | 45.8  | 49.4 | 47.4 | 45.0 | 45.5  | 45.6  | 45.8  |
| 3 | 54.4 | 53.8 | 52.2 | 64.8 | 62.9 | 61.9 | 58.8  | 58.6  | 58.8  | 62.8 | 60.3 | 56.9 | 58.8  | 58.6  | 58.8  |
| 4 | 62.4 | 62.4 | 58.7 | 75.9 | 73.7 | 71.8 | 70.1  | 69.6  | 69.5  | 73.7 | 70.9 | 66.1 | 70.1  | 69.6  | 69.5  |
| 6 | 75.3 | 75.9 | 69.7 | 91.6 | 89.3 | 86.6 | 87.4  | 87.8  | 86.6  | 88.8 | 86.1 | 82.7 | 87.4  | 87.8  | 86.6  |
| 8 | 84.9 | 85.7 | 79.5 | 97.9 | 96.5 | 95.0 | 96.3  | 96.1  | 97.1  | 95.3 | 93.9 | 91.0 | 96.3  | 96.1  | 97.1  |
| 10 | 90.7 | 90.9 | 86.8 | 99.1 | 97.7 | 97.4 | 98.5  | 98.3  | 100.6  | 97.5 | 96.3 | 97.1 | 98.5  | 98.3  | 100.6  |
| 12 | 93.7 | 92.3 | 90.9 | 99.2 | 97.8 | 97.8 | 98.8  | 98.8  | 100.8  | 97.6 | 97.1 | 99.3 | 98.8  | 98.8  | 100.8  |
| 16 | 94.8 | 93.3 | 94.4 | 99.3 | 98.0 | 98.1 | 98.8  | 98.7  | 99.9  | 98.8 | 97.7 | 100.2 | 98.8  | 98.7  | 99.9  |
| 20 | 95.2 | 93.2 | 95.0 | 99.4 | 98.0 | 98.2 | 98.5  | 98.3  | 100.8  | 97.8 | 97.8 | 99.3 | 98.5  | 98.3  | 100.8  |
| 24 | 95.5 | 93.3 | 95.0 | 99.7 | 98.1 | 98.4 | 98.5  | 98.4  | 100.9  | 98.4 | 98.0 | 100.0 | 98.5  | 98.4  | 100.9  |

# Figure S2. The in vitro release behaviors: IMM-H014 ER tablets in five different dissolution media; 0.01 N HCl→pH7.5 phosphate buffer saline （A），0.01 N HCl（B），pH 4.5 acetate buffer extraction procedure （C），water（D），pH 6.8 phosphate buffer saline（E）; three batches of IMM-H014 ER tablets (n = 12)