**METHOD(S)**

**Itraconazole:**
- **Extraction:** Stability of itraconazole was shown in plasma extracts by dilution in H2O at 40°C and 25°C, with no significant differences.
- **Internal Standard:** D8: 539.1 → 82.3

**Paroxetine:**
- **Extraction:** Stability of paroxetine was shown in plasma extracts by dilution in H2O at 40°C and 25°C, with no significant differences.
- **Internal Standard:** D8: 335.4 → 197.2

**Cimetidine:**
- **Extraction:** Stability of cimetidine was shown in plasma extracts by dilution in H2O at 40°C and 25°C, with no significant differences.
- **Internal Standard:** D8: 253.0 → 159.1

**Moxifloxacin:**
- **Extraction:** Stability of moxifloxacin was shown in plasma extracts by dilution in H2O at 40°C and 25°C, with no significant differences.
- **Internal Standard:** D8: 256.5 → 162.1

**Valproic Acid:**
- **Extraction:** Stability of valproic acid was shown in plasma extracts by dilution in H2O at 40°C and 25°C, with no significant differences.
- **Internal Standard:** D8: 256.5 → 162.1

**RESULT(S)**

- Accuracies and precision better than ±15% (≥ 20% at LLLOQ).
- Demonstrated selectivity and stability in the presence of co-administered drug.
- Reproducibility of results was ±3.0% to 7.6% for paroxetine, ±2.3% to 5.0% for cimetidine, and ±2.1% to 4.4% for moxifloxacin.
- Methanol (MeOH) precipitation was used in the validation process, followed by dilution in H2O and H2O/MEOH.
- Dynamic range for all compounds was 250.0 ng/mL to 25000 ng/mL.

**CONCLUSION(S)**

- Methods were developed and validated for simultaneous analysis of proprietary drug candidates with itraconazole, paroxetine, cimetidine, moxifloxacin, and valproic acid by HPLC-MS/MS.
- Methods are robust, simple, selective, and rapid with a run time of 6.2 - 6.8 minutes.
- Validation stability and selectivity for analysis of a novel drug candidate in the presence of the co-administered drugs in compliance with the 2018 FDA Guidance for the Validation of Bioanalytical Methods.
- Successfully applied to analyze clinical pharmacokinetic study samples:
  - 5084 plasma samples analyzed across five analytes.
  - 93% batch passing rate.
  - Performed within a 1 month turnaround after receipt of final shipment.
  - Demonstrated reproducibility upon incurred sample repeat (ISR) analysis.

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**Figure 1:** Itraconazole

**Figure 2:** Paroxetine

**Figure 3:** Cimetidine

**Figure 4:** Moxifloxacin

**Figure 5:** Valproic Acid

**Table 1:** Validation Summary