A Comprehensive Dataset of Pharmacokinetic Parameters for Recommended Doses of Drugs: Enabling Drug Repositioning and Pharmacological Analysis

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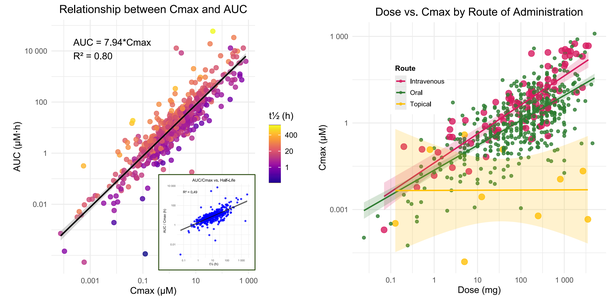
Background

Comprehensive knowledge of the pharmacokinetic (PK) properties of drugs is crucial for successful drug repositioning. Connecting in vitro efficacy data with in vivo dosage information requires detailed PK data. While PK information is available from various sources, the lack of a centralized, comprehensive database with sufficient detail hinders the evaluation of drugs for repositioning.

Existing resources often provide an overview of the drug pharmacokinetic/pharmacodynamic (PK/PD) profile but may not include the necessary details to establish a clear connection between dose, toxicological profile, and PK properties.

To address this gap, we present a dataset that contains major PK parameters for recommended doses of drugs.

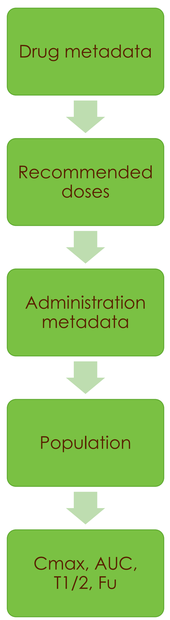
Relationship between PK parameters



Cmax exhibit strong correlation with AUC. Deviation from ideal correlation is mostly explained by t1/2 as shown in the inset.

PK parameters and molecular descriptors

LogP has strong negative correlation with fraction unbound which in turn is negatively associated with T1/2. Lipinski rule of 5 violation is associated with higher T1/2; the effect on other PK parameters (Cmax, AUC) and recommended dose is minimal.



Drugs:

- 637 drugs from NCATS collection
- Approved & Investigational drugs
- 51 target class
- Small molecules & peptides

Dose:

- Recommended dose from FDA labels
- Dose tested in Phase III on highest number of patients
- MTD, RP2D

Administration metadata:

- Frequency of administration
- Single / multiple administration
- Route of administration

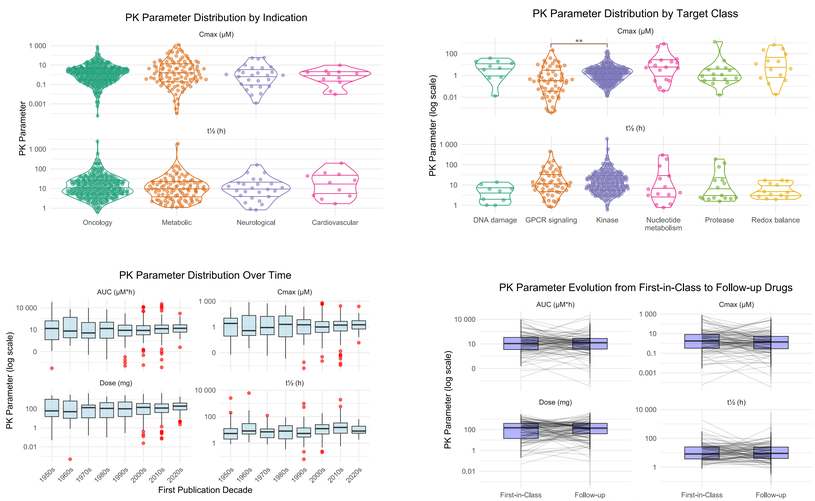
Population

- Population size
- Health status
- Food status

Sources

- Regulatory documents (reviews, labels)
- High-impact scientific articles
- High-impact reviews
- Other experimental data

PK parameters distribution



No significant difference in PK distribution was observed for indications (KS test + Bonferroni). Cmax for Kinases-targeting drugs was significantly (p = 0.01) higher than for GPCR targeting drugs. Distribution of PK parameters except $t_{1/2}$ became tighter with publication decade (Cmax, AUC, Dose - all p<0.01, 1980s vs 2010s).

Conclusions

The presented dataset provides a centralized and comprehensive resource of pharmacokinetic parameters for recommended doses of over 600 drugs. By integrating detailed PK data with drug properties, development stages, and therapeutic modalities, this dataset enables the establishment of critical connections between in vitro efficacy and in vivo dosage information.

The analysis of PK parameter associations and distributions offers valuable insights for drug repositioning and development strategies. Ultimately, this dataset has the potential to streamline drug repositioning efforts and accelerate the identification of new therapeutic applications for existing drugs.