

Pharmacokinetic Interactions

Distribution:

- Displacement from protein-binding sites **results in increased free or unbound fraction temporarily**, but it falls due to enhanced elimination or distribution (clearance).
- Therefore, there are only **few clinically important interactions due to protein binding displacement**, particularly for **highly protein-bound drugs** and **those that are NON-restrictively eliminated** especially when administered parenterally.
- Examples: Phenytoin, Lidocaine.

Pharmacokinetic Interactions

- Drugs whose hepatic extraction ratio exceeds their unbound fraction in plasma are **non-restrictively eliminated**.
- Drugs whose hepatic extraction ratio is smaller than their unbound fraction in plasma are **restrictively eliminated**.