

PHARMACOKINETICS

Plasma protein binding

Drug molecules circulating in blood are either bound to proteins and lipids or are freely available. The extent of protein binding may impact the efficacy and toxicology of a drug as it is generally believed that the free drug concentration drives the therapeutic outcome¹. Equilibrium dialysis is the commonly used technique for plasma protein binding studies².

Species: *Mus musculus* (Swiss)

Main read-out: % unbound drug

Drug concentration: upon request

Validation Data

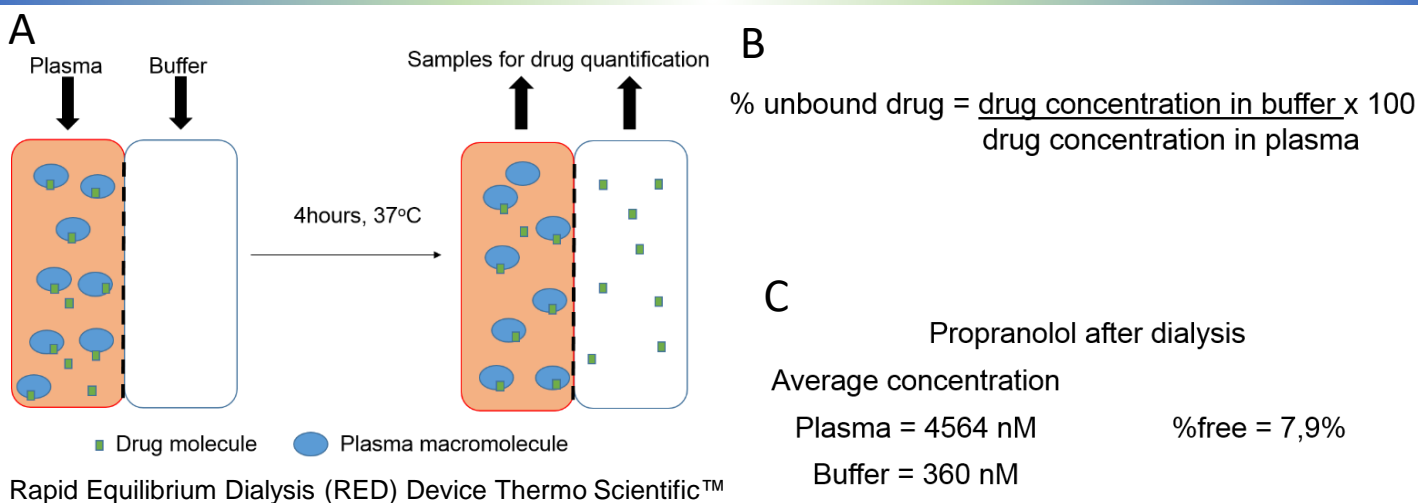


Figure: (A) Schematic description of the dialysis system. Propranolol was added to the plasma compartment of the dialysis system at a 5µM concentration. Drug that is binded to plasma macromolecules stay in the plasma compartment and the free drug can cross the dialysis membrane to the buffer compartment. After 4h, propranolol was quantified in both plasma and buffer compartments. Using the formula showed in (B) and the concentration values obtained, showed in (C), the calculated free propranolol percentual was 7,9%, what is in accordance with literature values³.

All in vitro experiments are performed in triplicate. Mice colony originated from Charles River Laboratories is breed and maintained in SPF conditions. Raw data are inspected by quality assurance unity. The experimental procedures were approved by the CIEnP Committee on the Ethical Use of Animals.

References:

- 1 -Di L, Breen C, Chambers R, Eckley ST, et al. Industry Perspective on Contemporary Protein-Binding Methodologies: Considerations for Regulatory Drug-Drug Interaction and Related Guidelines on Highly Bound Drugs. J Pharm Sci., 106(12):3442-3452, 2017.
- 2-Buscher B, Laakso S, Mascher H, et al. Bioanalysis for plasma protein binding studies in drug discovery and drug development: views and recommendations of the European Bioanalysis Forum. Bioanalysis. 6(5):673-82, 2014.
- 3-Waters NJ, Jones R, Williams G, Sohal B. Validation of a rapid equilibrium dialysis approach for the measurement of plasma protein binding. Pharm Sci. 2008 Oct;97(10):4586-95.

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