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Improved diffusion cell for drug binding and release studies

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The binding of a drug with blood plasma proteins critically influences its bioavailability for performing its therapeutic activity. In this context, drug binding and release studies are the preliminary and essential steps which determine the dose as well as sub-therapeutic and supra-therapeutic concentration of the drug. Determination of plasma protein binding of drugs is thus an important tool in pharmacokinetic studies. It plays a key role in the drug discovery process by enabling rapid screening of new chemical entities. The Franz Diffusion Cell is a standard apparatus used worldwide for such studies. Several innovations have taken place in which the binding and release studies have been made faster and simpler. Prominent amongst these are the 96-Well diffusion cells, which not only permit use of minimal quantities of plasma, but also enable automation and easy handling of samples. However, they are quite expensive and also require sophisticated handling accessories e.g. micropipettes/multichannel pipettes. They are generally affordable by contract research organizations where high-throughput screening takes place. They are not suited for teaching, training and research purposes where each student has to perform individual practical experiments. Thus, a simple, affordable and efficient diffusion cell is needed than the Franz Diffusion Cell. The new diffusion cell "Small Wonder-Lyzer" (US PATENT NO. 6368509, Indian Patent No. 1997211, www.wonderlyzer.com) comprises a semi-permeable cellulosic membrane sac which can be detachably attached to a volumetrically graduated plastic container, made of non-stick plastic. The plasma and drug solution are poured into the sac, which is then suspended in buffer by means of a non-floating holding plate. Owing to easy sample loading, the cell can also be used for performing studies with urine and blood. The free drug diffuses out through the membrane and can be easily quantitated, which gives a measure of the bound and unbound drug. The apparatus is affordable, easy to handle and has a small footprint. It overcomes limitations of the Franz Diffusion Cell and offers a simpler alternative for drug binding and release studies. Studies have shown that the plasma drug binding values obtained using the new diffusion cell, are as per reported values.

Keywords: Drug Binding, Drug release studies, Pharmacokinetics, Plasma protein binding, Diffusion Studies, 96-Well Diffusion Cells, Franz Diffusion Cell, Drug Discovery



Figure: Small-Wonder-Lyzer