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Portions of this article may be reprinted by Dr. Gal at a later date.

New Automated Franz Cell Sampling System Interfaces with Waters Dissolution HPLC System

by Bill Hanson, Hanson Research Corporation, Chatsworth, CA

Introduction

In vitro studies on the mechanism and absorption rate of drugs and ointments through the skin are extensively employed in the pharmaceutical and environmental fields. Pharmaceutics and pharmacokinetics are concerned with the safety and efficacy of delivery of therapeutic molecules, and environmental chemists are concerned about the absorption of toxic materials through the skin.

Technology

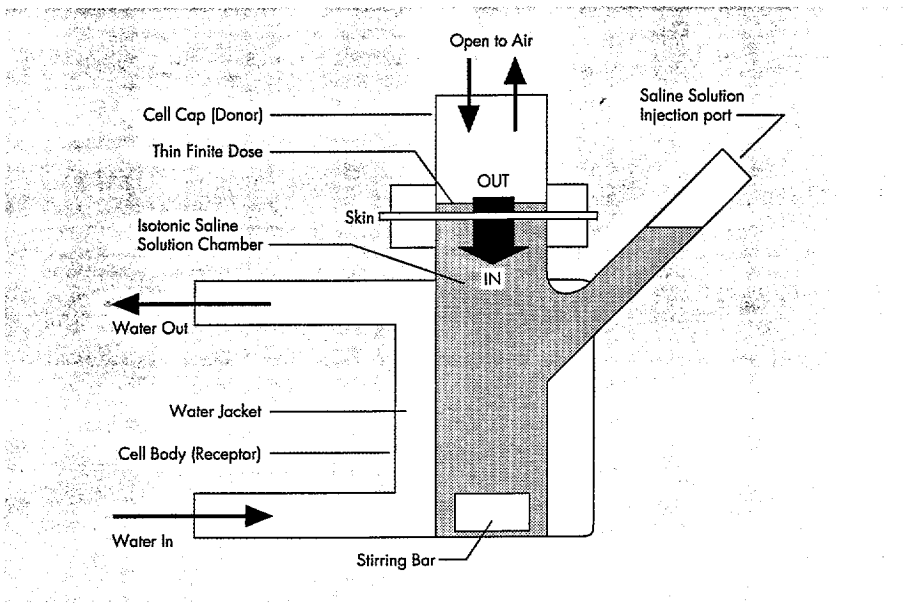
The basic laboratory experimental apparatus consists of two fluid phases separated by skin or an artificial membrane. The ingredient being studied is on the donor side of the membrane and an appropriate receptor solution, often isotonic saline, is on the other. The rate and means of drug transfer are studied.

A variety of models for this apparatus have been proposed. Three are in common use: the Franz cell , a side by side cell in which the membrane is located between two well stirred liquid chambers, and the flow through cell in which the receptor saline is pumped past the membrane. In all models certain parameters must be closely controlled. These include the surface area of the membrane, the skin temperature (normally 32°C,) and the agitation of the receptor solution.

The Franz Cell is popular in many of these studies. A schematic of a typical Franz cell is shown in Figure 3[1]. In manual operation an aliquot is removed from the sampling port with a syringe and an equivalent volume is replaced in the same manner. Typical membrane diameters range from 5-25 mm and cell volumes from 3-10 mL.

(continued on page 4)

Figure 3: Schematic of a Typical Franz Cell



A donor drug substance is placed on the skin or artificial membrane. Samples of the saline solution are analyzed with respect to time to determine the rate of drug transfer.[2]

Experimental Technique Restraints

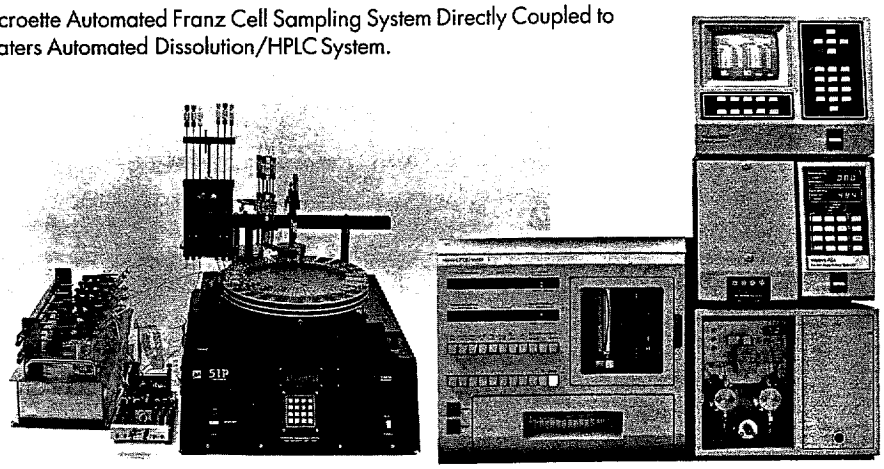
The Franz cell, the side by side cell and the flow through cell are closed systems. Careless sample withdrawal may introduce air bubbles which collect on the membrane changing the receptor solution contact area and distorting transfer data.

In addition, these systems generally limit the volume of sample aliquot to less than 800 µL. This constraint coupled with low concentrations limits the use of conventional UV detection. HPLC analysis methods are used almost exclusively. The frequent inclusion of excipients and polymers in the sample to modify transdermal perfusion may lead to difficulties in quantitation of active ingredients by direct spectrophotometric methods. HPLC offers a convenient solution to this problem. It provides highly efficient separations and detector options for the most demanding sample matrixes.

Automating Franz Cell Sampling

Surveys of the characteristics of massive numbers of transdermal formulations is common. Typically a test may include 6 to 24 test cells with as many as 8-25 sampling intervals, 30 minutes to an hour apart. Manual sampling imposes an impossible work load drastically restricting progress of these research programs.

Microette Automated Franz Cell Sampling System Directly Coupled to Waters Automated Dissolution/HPLC System.



In the completely automated mode, Franz cell samples are removed by the Microette and dispensed into empty vials located in its carousel. Immediately afterward, these vials are pressurized, transferring the samples directly into the active Waters 712D Autosampler for subsequent HPLC analysis.

A new automated sampling system, the Microette™ has been successfully developed and tested for the past three years. Using a sophisticated sampling technique under microprocessor control, the Microette can automatically withdraw 200-800 µL of sample from sets of six Franz cells at programmed intervals.

Complete automation of the analytical train is accomplished by interfacing the Microette with the Waters automated 610/600E PowerLine™ Automated Dissolution/HPLC system. The Microette operates on command from the Waters 610/600E PowerLine System Controller. The Microette withdraws samples at programmed intervals from six Franz cells and deposits them in its carousel. These samples are then immediately transferred into the carousel of an active Waters 712D WISP™ Autosampler while the system is analyzing previously collected samples or calibration standards. Coordination and timing of sample collection and HPLC analysis is achieved by the PowerLine system controller with priority placed on sample acquisition from the Franz cells over that of HPLC injections. Once sample acquisition from the Franz cells and sample transfer to the 712D WISP is complete, the PowerLine system controller then proceeds with the scheduled HPLC analysis protocol.

Percutaneous absorption studies requiring HPLC analysis can now be completely automated. By combining the unique sampling capabilities of the Hanson Microette and the sophisticated microprocessor controlled sample handling of the Waters Automated Dissolution/HPLC system, reliable unattended percutaneous absorption studies can now be realized.

1. Schematic courtesy Crown Glass Co., Somerville, NJ

2. T.J. Franz, in Curr. Probl. Dermatol, vol. 7, pp.58-68 (Karger, Basel 1978)