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COMMUNICATIONS

Apparatus for measuring *in vitro* availability of liquid oral preparations

To examine the availability *in vitro* of phenethicillin from three commercially available liquid oral paediatric preparations, a suitable apparatus was required. Two of the preparations examined had an oily basis and the other was aqueous. With the oily preparations it is probable that *in vivo*, the drug must first dissolve in and then diffuse through the oily medium before partitioning into an aqueous receptor phase. In the *in vitro* situation, a separating layer or film is required to comply with this requirement. Further, the separating phase does not allow intermixing and subsequent emulsification to occur. Thus the interfacial contact area between the two phases remains constant.

As a first step, a simple dialysis sac apparatus was devised to meet this requirement. It was considered that more complex films would complicate the experiment at this stage.

The apparatus consisted of a dialysis sac, contained in a 250 cm^3 jacketted beaker (Fig. 1). Visking tubing (Union Carbide Corporation), size 20/32, flat width 2·5 cm, was used as the dialysis membrane after soaking in distilled water for at least 24 h before use. The membrane, B, was fitted into position over the base cylindrical section, C, and sealed by the base cap, D. The membrane was then fitted over the upper cylindrical section, A, so as to expose a length of 40 mm. The beaker contained 250 cm^3 of 0·2 mol dm^{-3} phosphate buffer, pH 7·0, maintained at 37° ± 1° by means of a heating coil and water pump assembly (Braun Thermomix), circulating heated water around the beaker.

An accurately measured sample was placed in the dialysis sac, which was immersed in the buffer so that the exposed membrane was just below the surface. Both the sample and/or the external fluid were stirred when required using a Caframo RZR1–64 stirrer. The beaker fluid was stirred by a rectangular metal paddle (15 mm × 28 mm) with the upper edge 30 mm below the surface of the buffer. A flat metal blade (3 mm × 35 mm) tapering to a circular shaft (2 mm diameter) positioned to a depth

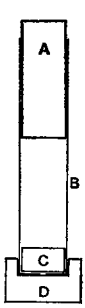

FIG. 1. Diagram of dialysis sac. A is the upper plastic cylindrical support. B is the dialysis tubing. C is the lower cylindrical plastic support. D is the base cap. The sample is placed inside the dialysis sac and the whole assembly is placed in the 250 cm^3 jacketted beaker.

of 106 mm in the cell was used to stir the sample. At preselected times the experiment was interrupted, the external solution quickly removed and replaced with fresh warmed buffer, ensuring operation under sink conditions. The removed fluid was sampled and assayed.

A rank order correlation was obtained from *in vitro* results when compared with previously obtained *in vivo* data (Marty & Hersey, 1975) for the three preparations.

The apparatus could be simply adapted for automation where a drug suitable for rapid analysis is used. Despite the correlation obtained and other encouraging results, such as the increased release of drug when the viscosity of one of the oily formulations was decreased, some criticisms of the model are pertinent.

The dialysis model is extremely slow compared with the rapid rate at which phenethicillin is absorbed *in vivo*. The rate of transfer in the model system may be unrelated to the *in vivo* absorption rate since different mechanisms are involved. Dialysis is due to a sieve-like effect, with transport occurring through pores in a heterogenous barrier. *In vivo* transport may be more closely simulated by homogenous barriers, such as polymeric membranes, where partitioning and diffusion through the membrane control the rate of transfer.

When comparing systems with different osmotic pressures in the *in vitro* model, it became apparent that solvent influx into the dialysis cell, thereby reducing the concentration gradient across the membrane, was having a considerable effect. This was particularly noticeable with an aqueous syrup when compared with an aqueous solution of phenethicillin, but also gave rise to some problems with the oily formulations. These difficulties may be overcome by using a solution of equivalent osmotic pressure in the external compartment or, more usefully, by dilution of the sample.

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REFERENCE

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