when the pH is lowered to 3. Since no significant particle growth has occurred, the relatively small primary particle size of the fresh gel gives a rapid rate of acid neutralization.

Phase II becomes more evident as the aluminum hydroxycarbonate gel ages. Both the primary particle size and the degree of aggregation increases during aging. Therefore, peptization becomes more important and the slow, second phase becomes more prominent. The rate of acid neutralization during phase III decreases during aging (day 2 *versus* day 155 in Fig. 2), which reflects the increase in primary particle size.

An understanding of the physicochemical processes required for the *in vitro* acid neutralization of aluminum hydroxycarbonate gel is necessary, because similar reactions occur in the GI tract when aluminum hydroxycarbonate gel is used as an antacid.

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Edward C. Scholtz
Mary I. Zapata
Stanley L. Hem[x]
Department of Industrial and Physical Pharmacy
Joseph R. Feldkamp
Joe L. White
Department of Agronomy
Purdue University
West Lafayette, IN 47907

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Simplified Method for Intravenous Dosing and Serial Blood Sampling of Unanesthetized Guinea Pigs

Keyphrases □ Blood sampling—serial collection from unanesthetized guinea pigs □ Guinea pigs—dosing and serial blood sampling without anesthesia □ Vacuum bleeding apparatus—serial blood collection from unanesthetized guinea pigs

To the Editor:

Ascorbic acid (vitamin C) levels can influence oxidative demethylation processes in the guinea pig (1), the only common laboratory animal unable to synthesize ascorbic acid endogenously (2). Thus, the guinea pig is an especially popular model for studying the effects of ascorbic acid on drug metabolism. Because of this, it is important to define methods for drug administration and repetitive blood sampling when using this species for pharmacokinetic studies. The following procedures were developed during a recent investigation of the effect of ascorbic acid on caffeine pharmacokinetics in young and aged guinea pigs.

A large towel was effective in quieting and immobilizing the animals during both drug dosing and blood sampling. The animals were prepared for dosing, by removing the hair over the injection site with an electric clipper. The prominent superficial vein on the medial side of the thigh (the medial saphenous vein) was used for all drug injections. The injection site was dabbed with ethanol and then the vein was enlarged using a finger to block venous return, and a small (21 gauge) needle was inserted in the direction of blood flow. A small quantity of blood was drawn *into the* 1-ml syringe to ensure correct insertion of the needle in the vein. Following a bolus injection of the drug solution, the needle was withdrawn quickly and pressure placed on the puncture with a finger to prevent venous backflow and avoid loss of some of the injected dose.

The method used here for repeated blood sampling was modified from that of Dolence and Jones (3) and found to be highly effective, producing a minimum of stress or pain in the guinea pigs. Similar to the procedure for caffeine dosing, the guinea pigs were wrapped in a towel exposing only the hind legs, which kept them comfortable yet immobilized. The leg not used for drug injection was extended and the hair removed using an electric clipper. A thin layer of silicone grease[1] was applied to the leg to form a tight seal with the vacuum bleeding apparatus and to prevent loose hair from contaminating the blood sample. One of the toenails was clipped, cutting into the vein and producing a flow of blood. Using this method alone only a small quantity of blood could be collected before coagulation stopped the flow. To circumvent this problem the prepared leg was positioned in the bleeding apparatus, as shown in Fig. 1, and the vacuum adjusted to produce a steady blood flow. The blood was collected in a 3-ml heparinized tube attached to the bottom of the vacuum-bleeding apparatus with a plastic[2] collar. The vacuum was adjusted to either increase or decrease the blood flow.

[1] Dow Corning, Midland, MI 48640.
[2] Tygon (R3603) tubing, Cole-Parmer, Chicago, IL 60648.

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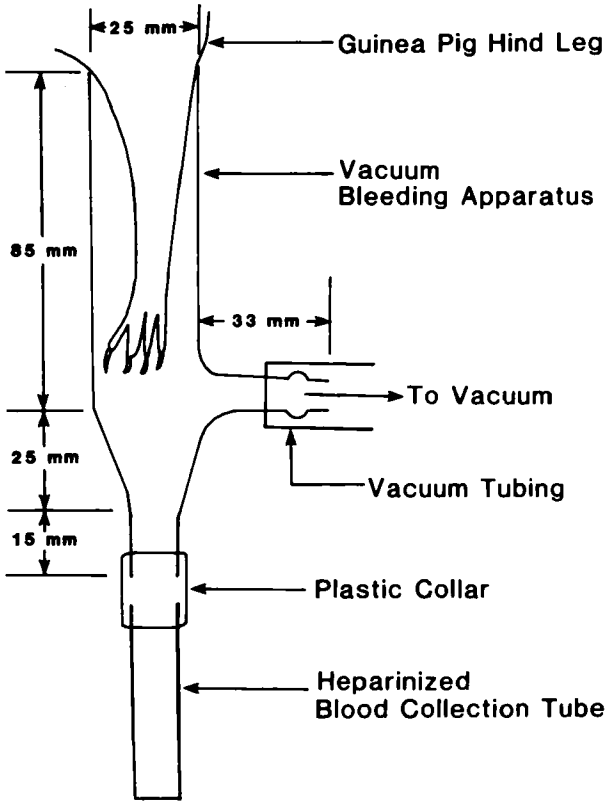

Figure 1—*Schematic diagram of the vacuum bleeding apparatus.*

When a 1- to 2-ml volume of whole blood was collected for each timed sample, the vacuum was turned off and the leg carefully removed from the apparatus. Bleeding usually ceased promptly, but it was sometimes necessary to place a gauze bandage over the toenail until all bleeding had stopped, usually within 1 min. For repeated blood collection from the same animal the nail was cut progressively more proximally at each sampling; the nails on both legs were used. The guinea pigs were not distressed by a sampling of up to 3 ml, and since no anesthetic was used, the animals had normal mobility when returned to their cages. The problem of blood clotting in the collection apparatus was minimized by using silicone grease on the inside glass surfaces.

Previous researchers have sampled guinea pig blood from the ear veins, penis vein, superficial thigh vein, jugular vein, orbital venous plexus and by the methods of heart puncture, indwelling vascular cannulation, cutting the toenail bed, and cutting the lateral saphenous vein or lateral metatarsal vein (4, 5). None of these methods proved completely satisfactory for the purposes of this study, since in most cases, an anesthetic was needed which could confound the observed results by affecting caffeine metabolism and/or plasma ascorbic acid levels (6, 7) if the study involved ascorbic acid supplementation, depletion, *etc.* We believe that the simplified procedure described here can be applied with similar success to studies involving other rodent species, in which anesthesia may be undesirable.

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David Hochman
James Blanchard[x]
Department of Pharmaceutical Sciences
College of Pharmacy
University of Arizona
Tucson, AZ 85721

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An Automated Sampling Device for Dissolution Testing

Keyphrases □ Dissolution testing—automated sampling device

To the Editor:

Many automated sampling devices have been designed for commercially available dissolution units[1]. The major criticism of some of these units is that the sampling probes remain in the dissolution medium during the duration of the test, thereby disturbing the hydrodynamics of the solution (1). This can cause dissolution results other than those intrinsic to the dosage form. We have designed a simple sampling device which eliminates this problem while still allowing the convenience of automation. The device is made from a commercially available air-actuated, solenoid-controlled valve[2] and brackets that can be easily made in-house. The design and orientation of the brackets are shown in Figs. 1 and 2. Dimensional and installational information is presented in Fig. 3. Air is supplied to the device at 20 psi. Either house air or an air pump can be used. The unit is connected to a computer-controlled pump-fraction collecter[2] which provides contact closure to the solenoid through its internal-timing sequences which also control the pump-fraction collector's prime, sample, and purge cycles. However, this unit need only be connected to a 110 V contact closure and external air supply to actuate the valve. Once actuated, any suitable multiple-channel pump and collector can provide samples.

As previously indicated, we have chosen a combination pump-fraction collector with computerized timing sequences. A program is entered using a hand-held pad, and at program-designated intervals contact closure is made, the device is actuated, and samples are collected during a three-part 60-sec sequence: for 20 sec the lines are washed with sample to waste; the sample tray is then advanced and the next 20-sec sample is collected; and for 20 sec the pumps reverse to purge the lines. The sample tray then

[1] Hanson Research Corp., Northridge, CA 91324; Applied Analytical Industries, Wilmington, NC 28403; Technicon Industrial Systems, Tarrytown, NY 10591.
[2] Bimba Manufacturing Co., Monee, IL 60449.

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