Improved Holder for Intrinsic Dissolution Rate Studies

By JOHN H. WOOD, JOHN E. SYARTO, and HERBERT LETTERMAN

An improved holder for use in rotational disk dissolution studies has been developed. The compression die becomes the rotating member. With it, the relative intrinsic dissolution rates at 37° in 0.1 *N* HCl with 430 r.p.m. rotational speed have been found to be caffeine monohydrate, 106, aspirin, 9.73, salicylamide, 12.3, and acetaminophen, 41.7 μmoles/cm.²/min.

STUDIES on the variation in inherent rate of dissolution of a drug with media, temperature, etc., are most conveniently performed from surfaces whose areas remain constant. Parrott (1) suggested the use of a spherical tablet, while Nelson (2) cemented flat disks to a strip so that only the one planar surface was available. Levy (3) modified this to insert and cement the disk perpendicular to a rotating shaft. Milosovich (4) used the compression die for the disk holder, but mounted this in a fixed position relative to the stirrer. Cooper and Kingery (5) have shown the desirability of the symmetrical system for purposes of dissolution kinetic comparisons. Levy (6) has applied their equations to his studies. The apparatus to be described here combines the advantages of the Levy technique with the Milosovich concept. It has been found to be useful over a period of several years with a wide variety of test conditions.

EXPERIMENTAL AND DISCUSSION

The apparatus is shown in Fig. 1. It consists of a $^5/_{16}$-in. punch cut down to $1^5/_8$ in. length. The $1^3/_8$-in. high die was machined from 316 stainless steel, $2^1/_8$ in. in diameter. A shoulder $^3/_8$ in. high and $1^1/_8$ in. in diameter was turned with 12 threads per inch. The bottom 0.25 in. of the die hole head was threaded at 18 per inch. The 0.25-in. shaft was brazed in place concentric with the axis of the 1.5-in. cup.

About 250 mg. of the drug to be studied is compressed in the die hole with a polished metal surface against the end face, a Carver hydraulic press supplying the desired pressure. The punch is left in place, and the upper cup is screwed on using a rubber gasket as shown to provide a liquid seal. The assembly is then mounted in any desired rotational motor assembly for dissolution studies. The rate of dissolution is followed by bulk analysis. The use of the threaded die hole prevents the disk from falling out even when dissolution is rapid or when the disk has a poor cohesive structure such that layer flaking would occur without the support walls. If necessary, as much as 75% can be dissolved before the disk falls free. Normally, dissolutions are made in 250 ml. of solution contained in a 400-ml. beaker, the apparatus being immersed about 1.5 in. Linear plots of dissolution with time result in the early time period when concentrations are very dilute relative to saturation. For the initial portions of the dissolution, the planar surface is still intact and not subject to any erosive tendency.

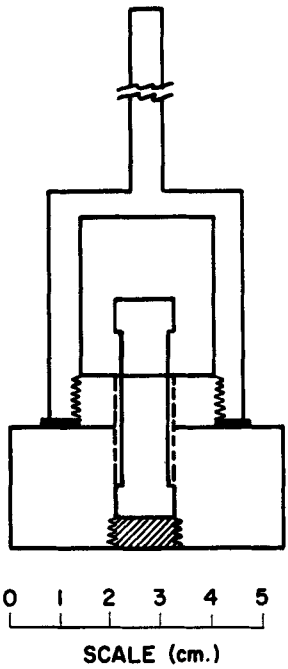

Fig. 1.—Scale drawing of compression die assembled for use in rotational dissolution.

As with the Levy (3, 6) technique, the dissolution rate is a function of the rotational speed as implicit in the Cooper-Kingery expression (5).

The relative dissolution rates measured for four compounds are given in Table I.

TABLE I.—INITIAL DISSOLUTION RATES OBSERVED IN 0.1 *N* HCl AT 37°C. WITH 430 r.p.m. ROTATIONAL SPEED

Compd.	Dissolution Rate, μmoles/cm.²/min.
Caffeine monohydrate	106
Aspirin	9.73
Salicylamide	12.3
Acetaminophen	41.7

Received February 26, 1965, from the Research and Development Laboratories, Bristol-Myers Products Division, Hillside, N. J.
Accepted for publication May 10, 1965.

REFERENCES

(1) Parrott, E. L., Wurster, D. E., and Higuchi, T., *J. Am. Pharm. Assoc., Sci. Ed.*, **44**, 269(1953).
(2) Nelson, E., *ibid.*, **47**, 297(1958).
(3) Levy, G., *J. Pharm. Sci.*, **51**, 58(1962).
(4) Milosovich, G., *ibid.*, **53**, 484(1964).
(5) Cooper, A. R., Jr., and Kingery, W. D., *J. Phys. Chem.* **66**, 665(1962).
(6) Levy, G., *J. Pharm. Sci.*, **52**, 1039(1963).