

medium quickly but four of the products had  $T_{50\%}$  values in excess of 120 minutes. One of the four products failed the disintegration test but the remaining three would be legally acceptable.

To check the validity of our dissolution test, we administered three of these products to three subjects and one patient. The subjects were also given a pharmaceutically acceptable product. After we had completed our blood analyses, we plotted blood curves and then calculated areas under the curve for each of the products. We then calculated a product index in the following way.

Area Under the Curve for Test Product

Product Index—

Area Under the Curve for Standard

We obtained the following results:

Product A (Standard)	=	1.00
Product E	=	0.76
Product X	=	0.55
Product W	=	0.25

This means that product E yields approximately 75 per cent of the amount of drug to the blood given up by Product A. In the case of Product W, the amount that was released to the blood was so low that the patient would have received equal relief from two Life Savers.

We concluded, therefore, that at least seven of the 23 brands of phenylbutazone tablets were significantly different in one respect or another from those that were uniform and released drug quickly to a test medium or to the blood. This means that 30.4 per cent of the products examined were not equal to the best brands available to the profession.

## 2. Prednisone Tablets-

In 1963, Campagna, et al., (J. Pharm. Sci., 52, 605 (1963) reported the following and I would like to quote from their paper.

"A 25 year old white married female of Mediterranean ancestry has been under the care of one of us (FAC) for approximately five years. Her clinical diagnosis was familial Mediterranean fever. The prompt use of oral prednisone in amounts of 20 mg. in a 24 hour period for the first 2 or 3 days would promptly abort the clinical symptoms. . . The patient's prescription had been written under the generic name "prednisone". On one occasion, after 72 hours of 5 mg. four times a day, the patient had no clinical effects from the medication. It was discovered. . . that a different brand of prednisone had been dispensed. . . The patient was immediately transferred to the brand of prednisone used previously and again within 24 hours there was almost complete resolution of the clinical syndrome."

The late Dr. Nelson, a pioneer and expert in the field of biopharmacy, determined the dissolution characteristics of both products. Both products disintegrated in less than 6 minutes. However, the  $T_{50\%}$  value for the clinically active preparation was 4.3 minutes and that for the clinically inactive product was 100 minutes.