of eriodictyon. The small proportion of water added stabilizes the preparation at all ordinary temperatures.

The next most pleasant preparation, perhaps, is a simple solution of the salt in syrup of orange. This is the formula of the German, Austrian and the Hungarian Pharmacopœias.

To the physician, the prescribing of this formula offers the advantages of a preparation of a fair degree of palatability of known composition. The above formula is, therefore, submitted to the pharmaceutical profession with the request that it be tested and criticized, to the end that the National Formulary may contain the best possible preparation of this medicinal agent.

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THE VARIABILITY OF PHARMACEUTICAL PREPARATIONS.*

BY H. B. HAAG AND L. E. JARRETT.

Attention has been called upon several occasions to the variability of certain pharmaceutical preparations. Many of these studies have been concerned with drugs very liable to deterioration, such as the liquid preparations of digitalis. The fact that discrepancies have frequently been found should be a challenge to those interested in professional pharmacy and public health. Clinicians have taken some of these observations seriously, so seriously, in fact, that in increasing numbers they are turning to certain types of proprietary preparations in the hope that in these they will find, at least, uniformity. Needless to say manufacturers have apparently not been particularly loath to take advantage of this situation; we have proprietary names for almost every conceivable drug. The sad part of this state of affairs is that much of the blame probably rests with the pharmacist; by neglect in exercising proper professional care of his legitimate business, he is gradually reducing his calling to that of a middle man, pouring from this or that container a preparation which he, by right of his training, should have compounded. This paper is offered with the view of presenting additional information as to the quality of some of the common official drugs and their preparations, with the hope that it will stimulate a lagging professional spirit. While the results herein reported are based upon studies made upon specimens collected throughout Virginia, there is no reason to believe other than that similar results would have been obtained had the samples been collected in any other locality.

Through the generous coöperation of the secretary of the Virginia State Board of Pharmacy, plans were made to collect, in various sections of the state, specimens of some of the more commonly dispensed official drugs, and particularly those which would lend themselves relatively easily to analytical study. Ten samples of each specimen were to be obtained from different pharmacies. The original plan was to obtain samples of the following: Tincture of Digitalis, Diluted Hydrochloric Acid, Spirit of Nitrous Ether, Liniment of Camphor, Saturated Solution of Potassium Iodide, Spirit of Camphor, Sodium Nitrite, Tincture of Iodine, a

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percentage ointment, and Solution of Hydrogen Peroxide. Up to the present time analytical studies have been made upon the first four. This laboratory was supplied with these preparations in the original one-fluidounce bottles, with the original label substituted by a number, so that at no time was the source of any of these specimens known.

TINCTURE OF DIGITALIS.

Ten specimens of Tincture of Digitalis were received from the secretary of the Virginia State Board of Pharmacy in December 1929, and the following tests were made shortly after receipt in this laboratory. In addition, two other preparations, numbers three and five, were secured from the Drug Room and Hospital Pharmacy of this institution, respectively. These were all assayed biologically by the Cat Method of Hatcher and Brody (1). As will be recalled, judged by the "cat method" a standard preparation is one which, when run continuously into the femoral vein of a cat, will produce death in about ninety minutes in a quantity corresponding to 100 mg. of the leaf per Kg. of bodyweight. This amount per Kg. is called a "cat unit" and it follows that the smaller the numerical figure representing the "cat unit" the more potent the preparation. It is of course necessary to arrive at this figure from the average of several assays. Determinations were made of the hydrogen-ion concentration of most of the specimens by means of the quinhydrone method. Table I illustrates the results of these studies on each specimen.

TABLE I.

Specimen number.	Activity (mg. × Kg.).	p_H.	Specimen number.	Activity (mg. × Kg.).	p_H.
1	76.0	4.06	7	126.0	4.4
2	99.0	4.15	8	137.0	4.15
3	106.0	..	9	142.0	5.5
4	109.0	4.32	10	143.0	4.38
5	110.0	..	11	164.0	4.32
6	115.0	4.66	12	267.0	4.32

It becomes immediately evident from this tabulation that the various tinctures show great differences in activity, and that there appears to be no definite relationship between the hydrogen-ion concentration and the physiological activity. Of the twelve specimens assayed only about fifty per cent were within the standards set for a good preparation. These findings resemble those presented in a recent similar study by Ward (2). Attempt was made to assay these specimens using frogs, but the results in the main were not encouraging; there was often wide variation among frogs when tested with the same specimen and, even more frequently, marked discrepancies when the results so approximated were compared with the tests obtained upon cats. These difficulties encountered when using the frog method have frequently been stressed in the literature bearing upon the subject. In spite of the fact that the glucosides of digitalis are hydrolyzed by acids, the most active specimen was the one with the highest hydrogen-ion concentration. Of course the question of the age of the samples probably plays a great part, and it is easily conceivable that the more potent tinctures might have been of the most recent manufacture. The figures indicating the hydrogen-ion concentration for these specimens are in keeping with similar studies made by

other investigators (3, 4, 5, 6). While it has been shown that most tinctures of digitalis deteriorate slowly, it is also known that some tinctures deteriorate rather rapidly. Hence it would appear advisable for pharmacists who do not have a great demand for Tincture of Digitalis to purchase this preparation in small quantities so as to refresh their supply at short intervals. Better still it would be to persuade physicians to use the powdered leaf, which is known to be stable for years.

DILUTED HYDROCHLORIC ACID.

On the twenty-first of August 1929, ten one-fluidounce specimens of Diluted Hydrochloric Acid were received. These were assayed according to the U. S. P. X requirements on August twenty-seventh, 1929, with the results as given in Table II. In addition, specimens numbers three and seven were obtained from the Drug Room and Hospital Pharmacy of this institution, respectively.

TABLE II.

Specimen number.	Per cent HCl.	Specimen number.	Per cent HCl.
1	2.9	7	10.90
2	9.25	8	11.6
3	9.74	9	11.9
4	10.09	10	12.8
5	10.40	11	12.8
6	10.90	12	12.9

The U. S. P. X states that Diluted Hydrochloric Acid shall contain not less than 9.5% or more than 10.5% HCl. It will be observed that, with the exception of specimen number one, most of the preparations range either within or close to the official requirements. The last three or four are somewhat higher in their HCl content than they should be, and while for practical purposes this difference is negligible, there is little excuse for this preparation showing such variation. It is almost inconceivable how one could misinterpret the simple directions of the pharmacopœia for preparing Diluted Hydrochloric Acid, yet apparently some gross misinterpretation must have been exercised when number one was prepared. It might be argued that a mistake of this nature, inasmuch as it does not result in a toxic product, should not be severely condemned. However, discrepancies such as this weaken the physician's regard for official preparations, and pave the way for the introduction of some proprietary drug.

SPIRIT OF NITROUS ETHER.

On the second of November 1929, ten one-fluidounce specimens of Spirit of Nitrous Ether were received, and on the next day they were assayed according to the directions in the U. S. P. X. At least two tests were made upon each one, and the potency judged from an average of the two assays. Table III shows the results so obtained.

TABLE III.

Specimen number.	Per cent ethyl nitrite.	Specimen number.	Per cent ethyl nitrite.
1	1.82	6	2.65
2	2.07	7	2.74
3	2.18	8	3.03
4	2.63	9	3.82
5	2.64	10	4.50

The U. S. P. X requires that Spirit of Nitrous Ether contain not less than 3.5% or more than 4.5% ethyl nitrite. Only two of the preparations assayed within the pharmacopœial requirements, the remainder being below the minimal standards. These findings are in harmony with the results frequently mentioned in pharmaceutical literature (7, 8, 9, 10). In addition to the above specimens an additional one was secured directly from a local manufacturing jobber. Upon analysis this was found to contain slightly above three per cent ethyl nitrite, but was not within the pharmacopœial limits.

LINIMENT OF CAMPHOR.

Ten specimens of Liniment of Camphor were received on March 10, 1929, and tested during the next several days. Three assays were made upon each sample, the tests being made as directed by the tenth revision of the Pharmacopœia. The average of these assays is given in Table IV.

TABLE IV.

Specimen number.	Per cent camphor.	Specimen number.	Per cent camphor.
1	18.1	6	19.3
2	18.3	7	19.5
3	18.6	8	19.7
4	18.9	9	20.0
5	19.3	10	22.0

The official requirement for Liniment of Camphor is that it should contain not less than 19.5% or more than 20.5% camphor. These specimens show the least variation of any tested, and as a whole approach more closely the pharmacopœial requirements. The fact that most pharmacists manufacture this preparation in their own laboratories makes these findings rather encouraging.

SUMMARY AND CONCLUSIONS.

Tinctures of Digitalis purchased from various pharmacies in Virginia show great variation in activity when tested by the Cat Method. There appeared to be no definite relationship between the activity of the tinctures and the hydrogen-ion concentration. Pharmacists are urged to purchase their supplies of Tincture of Digitalis in such quantities as to insure a fresh lot at short intervals.

Specimens of Diluted Hydrochloric Acid, while in the main of pharmacopœial potency, show variation in some instances. One specimen is cited which contained only about thirty per cent as much HCl as is required by the pharmacopœia.

Spirit of Nitrous Ether was found to be in most instances well below the U. S. P. X requirements.

Liniment of Camphor, of all the preparations tested, showed the most concordant assays.

In order to combat the inroads being made by proprietary preparations and in order to bring back to pharmacy its rightful heritage, it is urged that pharmacists exercise more care in the strictly professional side of their business.

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DR. FRANKLIN BACHE, CHAIRMAN OF U. S. P. REVISION COMMITTEE,* 1860.

BY CHARLES H. LAWALL.

Dr. Franklin Bache was a native of Philadelphia and a great grandson of Benjamin Franklin. His father was Benjamin Franklin Bache, editor of the *Aurora*, a Philadelphia newspaper, famed for its opposition to Washington and Adams and the Federalists. He was born in 1792. His early education was obtained in the private school of Dr. Wylie, after the completion of which he graduated from the University of Pennsylvania, first as a Bachelor of Arts, in 1810, and later, in 1814, as Doctor of Medicine. In this same year he became a Master Mason in Franklin Lodge 134 of Philadelphia, which had been named for his illustrious ancestor.

DR. FRANKLIN BACHE.

His first experience in medicine was obtained as surgeon's mate in the Army in which service he spent three years and had attained the full rank of surgeon at the time of his discharge.

He occupied several minor positions as physician to several Philadelphia prisons during the early years of his private practice. He became particularly interested in science in general and in chemistry particularly and, in 1819, he published a "System of Chemistry for the Use of Students of Medicine."

Along with Dr. Samuel Jackson, another celebrated young Philadelphia physician, he organized a Philadelphia branch of a medical association of national scope called the *Kappa Lambda* Society, founded in Louisville, Ky., in 1822 by Dr. Samuel Brown. This society had a great influence in promoting harmonious relations between physicians and raising ethical standards in the profession of medicine.

Dr. Bache became the first lecturer in chemistry, in 1826, in the Franklin Institute, which had just been founded two years previously, and which was then functioning as a teaching institution in the Arts and Sciences. He had previously

* Section on Historical Pharmacy, A. PH. A., Baltimore, Md., 1931.