THE QUALITY OF TINCTURE OF DIGITALIS DISPENSED BY PHARMACISTS.*

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In view of certain statements made in the Spring of 1930 at the hearings before the Senate Committee on Agriculture and Forestry on the quality of drugs dispensed by the pharmacists of the United States, the Board of Pharmacy of the State of New Jersey took steps to inquire into the situation as far as this state is concerned. One of the preparations which was said to be furnished to the public in sub-standard form was Tincture Digitalis.

The Board therefore decided to determine the quality of Tincture Digitalis furnished to retail druggists of New Jersey by various manufacturers, and also the quality of the Tincture Digitalis supplied to the public by pharmacists on the prescriptions of physicians.

Samples of Tincture Digitalis were purchased in original four-ounce containers directly from nine representative manufacturing and wholesale houses. In eight cases out of the nine, the product was labeled to meet the U. S. P. requirements. One sample, that of a wholesale house, was labeled "U. S. P. Eighth Revision." In view of the fact that the present U. S. P. is the Tenth Revision and that both the Ninth and Tenth Revisions required Tincture Digitalis to be biologically assayed, while the Eighth Revision did not, it appeared that this manufacturer labeled his product "U. S. P. Eighth Revision" in the expectation that he could escape responsibility for a biological assay. This product was the only one which was not labeled as having been biologically assayed. The other eight products bore a distinct statement on the label to the effect that the Tincture had been biologically assayed and found to meet the U. S. P. X requirements. One sample bore a date of manufacture, and one sample bore a date of test.

All of these tinctures were subjected to biological assay by an expert. It should be recalled that biological assay methods have not reached the state of perfection that is common to chemical assay methods. The U. S. P. standard for Tincture Digitalis makes due allowance for the variation in the reaction of test animals to this potent tincture. The standard prescribed is stated in part as follows: "Tincture Digitalis injected into the ventral lymph sac of a frog has a minimum systolic dose of not less than 0.0055 cc. and not more than 0.0065 cc. for each Gm. of body weight of frog." If we assume that a Tincture Digitalis having a minimum systolic dose of 0.006 cc. for each Gm. of body weight of frog is a 100% tincture, then the range of percentage as given in the Pharmacopœia is approximately from 92% to 108%. In other words, the upper limit, according to the U. S. P. X standard, would be a tincture of approximately 108% activity, and the lower limit, approximately 92% activity. Any tincture purchased in the open market, or any tincture dispensed on a prescription, which would come within the range of 90% to 110% could be considered, for all practical purposes, as meeting the requirements of the U. S. P. for physiological activity. This allows a total variation range of 20%.

The nine samples tested showed a range of activity from 83% to 108%. Two samples showed an activity of 83%. Three samples were 90% active. Two

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samples were reported 98% active, and the remaining two showed an activity of 108%. It will be seen, therefore, that only two out of the nine samples were appreciably below the lower limit of the U. S. P. standard of activity. One of these samples was the product labeled "U. S. P. Eighth Revision" and without a statement as to whether it had been biologically assayed. We can conclude from the results of this examination that seven out of nine products furnished by manufacturers to retail druggists in New Jersey were practically of U. S. P. quality.

When it is considered that Tincture Digitalis may deteriorate upon standing, it would seem justifiable to call the attention of manufacturers to the necessity for not only maintaining their product within the U. S. P. limits of activity, but also endeavoring to keep as far above the lower limit and as near to the 100% mark as possible.

It is interesting to observe that the product bearing the date of manufacture on the label was assayed three months and twenty-two days after the date of manufacture, and found to be 98% active. The sample purchased from the manufacturer who placed the date of test on the label was assayed one month and two days after the date of their test, and found to be 90% active. The system of placing the date of manufacture on the labels of products which are prone to deterioration is to be commended as being in the interests of the public health. When more definite information is available on the question of deterioration, it will be in the interest of the public health for manufacturers to exchange outdated original packages of pharmaceuticals on the same basis as biological products are now handled.

QUALITY OF TINCTURE DIGITALIS SUPPLIED BY PHARMACISTS ON PRESCRIPTIONS.

In order to obtain samples of Tincture Digitalis as dispensed on physicians' prescriptions by retail druggists in the regular course of their daily work, we presented twenty-four prescriptions, each calling for one fluidounce of Tincture Digitalis U. S. P., to twenty-four retail drug stores located in twenty of the twenty-one counties of the State of New Jersey. The identity of the ultimate recipient of the prescriptions was not revealed until the prescription had been compounded, delivered to the agent of the Board and paid for. The agent then divided the prescription, retaining one-half of it in the original container and sealing it with the seal of the Board, and leaving the other half with the druggist who filled the prescription, also sealing this with the seal of the Board at the same time. The original prescriptions were assayed by an expert according to the U. S. P. biological assay method. An additional check test was made in each case, using the Reed & Vanderkleed Guinea Pig Method.

The percentage of physiological activity in these prescriptions was calculated on the same basis as in the manufacturers' samples noted above. The activity in twenty-two out of the twenty-four prescriptions came practically within the upper and lower limits specified in the U. S. P. Five prescriptions had an activity of 90%; eleven prescriptions showed an activity of 98%; and six prescriptions showed an activity of 108%. One prescription was 120% active, or 12% above the upper U. S. P. limit, and one prescription was only 77% active, or 15% below the lower U. S. P. limit. It will be noted, therefore, that out of the twenty-four samples collected on prescriptions from retail druggists, only two were appreciably "off standard."

We communicated with each pharmacist within a few days of the date on which the prescriptions were filled, asking him to advise us whether or not he had manufactured the Tincture Digitalis himself, and if not, to give us the name of the manufacturer. Two of the twenty-four pharmacists did not reply to our communication. Two stated that they had made the tincture from Fluidextract of Digitalis by dilution. In one case the tincture thus prepared showed an activity of 98%, and in the other case it was 108%. Nineteen others stated that they had dispensed a manufacturer's tincture. One pharmacist stated that he had filled the prescription from a manufacturer's container, but as he had the tincture of several manufacturers on hand, he could not recall which manufacturer's product had been used in this particular case. By a peculiar coincidence, all of the manufacturers named by the retail druggists, with the exception of one, were included in the group whose products had been purchased direct and had been assayed by us.

The conclusions to be drawn from this investigation are that, in general, the pharmacists of New Jersey are receiving a good quality Tincture Digitalis from manufacturers and wholesalers, and that the public in turn is receiving a good quality Tincture Digitalis on prescriptions compounded by these pharmacists. Even though some of the samples of this tincture supplied were somewhat above and somewhat below the maximum and minimum standards designated by the U. S. P., the discrepancies were, in no sense, of a nature to endanger the health of persons requiring the action of this tincture. Claims to the effect that persons suffering from heart conditions requiring the use of Digitalis are dying because of the poor quality of Tincture Digitalis furnished by pharmacists, seem to be entirely unfounded in fact, as far as this investigation is able to disclose the facts.

A number of interesting observations in connection with this work could be made. In the first place, it seems advisable to caution pharmacists to read the labels on all preparations which they buy from manufacturers. There is still a tendency on the part of some manufacturers and wholesalers to make evasive statements on their labels, which may get the retail pharmacist into trouble.

Manufacturers who give pharmacists and physicians some idea of the age of the products which they dispense, by dating them, are to be commended.

No attempt was made in this investigation to select pharmacies which specialize in prescription work. The prescriptions for Tincture Digitalis were filled in the average type of corner drug store found throughout the State of New Jersey.

IBSEN AND PHARMACY.

Henrik Ibsen was apprenticed to a pharmacist, Jens Aarup Reimann, at Grimstad, in 1844, and remained with his successor, Lars Nielsen, until April 1850. The original pharmacy in which Ibsen spent six years has been replaced by a new building and is known as the "Ibsen House;" the fittings of the old pharmacy have been retained in the new premises. Ibsen wrote "Catalina" before discontinuing his pharmaceutical work, and gave to Norway and the world such plays as "Brand," "Peer Gynt," "A Doll's House," "Hedda Gabler" and "Ghosts"—Ibsen brought Norway back into the literary world and made men and women think.

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