

INFUSION OF DIGITALIS U. S. P.

CHAS. M. FORD, PH. G.

The following report is taken from the files of the Food and Drug Department of the State of Colorado, and was submitted by this writer in his official capacity as State Drug Inspector:

"The question of how the physiologic test upon a package of digitalis shall be regarded by the retail druggist has been brought to the attention of this office.

"Inasmuch as there is no official, chemical or physiologic standard for the drug, a strict construction of the law of this State requires that all official preparations be made according to the proportions laid down in the United States Pharmacopœia.

"In all probability, the next revision of the Pharmacopœia will contain physiologic tests for such potent drugs as cannot be valued chemically. It would therefore seem fair for the conscientious pharmacist to anticipate the action of the Committee on Revision and dispense such important a remedy as infusion Digitalis with a careful regard for toxicity and therapeutic powers as shown by trustworthy physiologic assays.

"A visit to a number of Denver stores shows that a principal source of supply for digitalis leaf is one British firm, who now place upon each container the strength of the drug, as compared with an arbitrary standard of their own. The reputation of the firm throughout the world merits for their standard and similar declarations the careful consideration of pharmacists and physicians."

Every pharmacist recognizes the necessity for standardization and rubrics of purity, especially for plant drugs. It is a well known fact that we have no chemical or physiological test for determining the toxic or therapeutic potency of some of our most important plant drugs, including digitalis and the U. S. P., is silent as to physiological tests.

The main object of a legalized authority, such as the U. S. P. and N. F. is to secure uniformity in the strength and character of official substances and preparations. Now in the case of digitalis, known to have a wide range of variation, in medicinal value, how is this uniformity to be secured? Obviously, not by adhering to the fixed proportion given for preparing infusion digitalis. Or will someone contend that the physician must observe this varying strength of an official preparation, at the bedside and regulate the dose accordingly?

Technically speaking, any deviation from official formulas is violation of law in the State of Colorado, but in the case of infusion digitalis, in the writer's opinion, a rigid compliance with the letter of the law is a flagrant violation of its spirit and purpose, and should not be countenanced in any well regulated pharmacy.

INFUSION OF DIGITALIS.

J. LEON LASCOFF.

For many years past pharmaceutical journals have given much room to the discussion of the subject of digitalis. Still, little or nothing has been mentioned about the infusion of this most important drug. Of all the infusions, that have

been prescribed and have not lost their use in therapeutics, digitalis is one of the most important, and yet it is the one, in spite of its great importance, to be abused the most.

Let us consider what the physician intends when prescribing this infusion. His object is to give the patient a preparation of digitalis that shall not contain all of the principles found in the powder, the tincture, and the fluidextract. He wants only those soluble in water. In order to bring this about, it is the duty of the pharmacist to manufacture an infusion and bear certain important facts in mind in doing so.

1. The quality of digitalis.
2. Method of preparation, utensils and time necessary.

(1) In selecting the leaves always purchase the one which costs the most, which bears the guarantee label and date of selection. Whether the leaves should be the first or second year's crop, wild growth or cultivated, are not to be considered in this paper, as the question is not yet definitely decided upon by authorities; but I have found through personal experience that the leaves purchased from Allen & Co. bearing the certificate label of purity and date, are the best for the manufacture of infusions; and I have come to this conclusion as the result of experiment by purchasing four different qualities of leaves at prices ranging from 50 to 85 cents per pound.

It may seem to be unethical to mention the aforesaid name of firm; still I am of opinion that such should not bear criticism in this case, as we are dealing with a drug, the action of which may influence the life of an individual, and as the firm actually guarantees its purity and selection and date, and as no other concern does so, I don't hesitate to recommend Fol. Digitalis Allen. If I am authentically informed that this is not the case I will gladly strike out the name.

(2) Just as important as is the quality of the leaves, so is the method of manufacture. One must always follow out the instructions of the U. S. P. and so pay strict attention to the utensils used and to the time occupied in making the infusion. Only porcelain or glass dishes should be employed; no metal or enameled dishes should be used for obvious reasons. After the preparation has been allowed to remain standing for one hour, well covered, the remaining leaves should be placed in cheesecloth and squeezed through in order to get out all possible strength, and then the entire liquid properly filtered. Although the U. S. P. requires the addition of alcohol, I think it could be just as well omitted if only for the reason that the pharmacist would not be tempted to make up a stock solution. Physicians frequently prescribe also Infusion digitalis, different strength, mentioning the quality of the leaves, and in such case alcohol should not be used.

I want at present to take the opportunity to criticise the contemptible habit of some pharmacists who make the infusion from fluidextract. It is true, that every drop of the extract represents one grain of the drug, but the fluidextract is made with alcohol and represents all the constituents of the original drug, just exactly what the physician does not want in his infusion. The therapeutic effects are entirely different than that intended by the prescriber. You are therefore doing

an injustice to the physician, patient and yourself. *Whatever is worth doing is worth doing well.*

And this most certainly applies in this case in which human safety is at stake. As an illustration of my remarks regarding the various qualities, grade and price of digitalis leaves on the market, I had examined by a physiological chemist, four specimens of the different grades and prices, with the result as follows:

	M. L. D.	Strength	Cost
(1)	12.3 Cc.	54%	.55 per pound
(2)	10.0 Cc.	67%	.65 per pound
(3)	10.0 Cc.	67%	.70 per pound
(4)	8.3 Cc.	80%	.85 per pound

which means that in Specimen 1, the poorest grade, it required 12.3 cc. of the infusion to kill a normal weight Guinea pig, and that the total percentage of drug strength compared to the tincture was 54 per cent.

Four, the best grade, required only 8.3 cc. of the infusion to kill the same size pig with the total per cent. of 80.

We see then that No. 1 is the weakest and cost the least, and No. 4 the strongest and cost the most, and yet the cost for 250 cc. is so trivial that it must be computed by fractions of 1 per cent. For example:

	lb	30.0	7.5	} To make 250.0 Cc.
(1)	55c	0.034	0.0085	
	lb	30.0	7.5	
(2)	85c	0.053	0.0133	

The difference of price of 250 cc. bottle of infusion is just 0.0048, or approximately one-half cent. If the saving is sufficient to cause the pharmacist to employ the inferior grade in preference to the more costly one, then it is time for him to close his establishment.

DISCUSSION.

MR. VANDERKLEED called attention to the fact that in making the infusion it was not possible to avoid getting some of the heart stimulating principles in it, but that these would not be present to the same extent in an aqueous infusion as in an alcoholic tincture, consequently it was possible for the physician to vary the effect by specifying the infusion in one case and the tincture in another.

MR. HOWELL did not accept the statement that infusion of digitalis has only a diuretic effect. In the making of a number of experiments on dogs and frogs it was necessary to deduct the effect of the alcohol in order to compare the infusion with the tincture.

Infusion of digitalis is decidedly more strong in its heart action than it is thought to be by some people.

MR. WILBERT hoped that the dangerous and misleading impression would not be created that the quality of digitalis depended entirely upon the price paid for the drug. The question of price has little or nothing to do with quality. The question of digitalis is an extremely complicated one and not to be solved offhand.

He stated that the Bulletins on Digitalis issued by the Hygienic Laboratory would justify different conclusions than those presented in the papers read. He hoped Mr. Lascoff would

eliminate therapeutic reference in his paper lest it be construed by medical men as an assumption on the part of pharmacists to say something about which they know little or nothing.

MR. GROFF stated that the earlier physicians who used digitalis employed only the leaves after they had been deprived of midribs and large veins. He thought it possible that such a drug would be more uniform in action than the whole leaves.

With regard to the use of therapeutic references, he thought that these should be given in colleges of pharmacy in the lectures on physiology, and that the lecturer should be a physician.

MR. RAUBENHEIMER said that the present U. S. P. does not state that the infusion must be freshly prepared, as it undoubtedly should. Many pharmacists seem to think that the addition of alcohol in the present formula gives them the right to keep the infusion on hands and dispense as wanted. The Pharmacopœia should definitely state that the infusion must be freshly prepared. He did not agree with Professor Lascoff as to the squeezing of digitalis leaves and filtering the infusion. Adding water through the leaves takes out practically all of the soluble principles.

MR. DUNNING preferred to make the infusion by pouring boiling water through the leaves, and after standing an hour pour through a funnel containing cotton, following with sufficient water through the leaves and cotton to make the required quantity, after the alcohol has been added.

In response to a question by Mr. Alpers as to the reason for the alcohol in the present formula, Mr. Hynson thought that it was to aid in keeping the infusion until used by the patient.

MR. WILBERT said it was the remnant of the practice in which brandy was added to make the preparation more palatable, and that this had been misconstrued into a preservative.

MR. LASCOFF stated with reference to the diuretic action of the drug that he had communicated with at least twenty physicians, and that they had endorsed the statement made.

MR. ALPERS stated that if it was true that the object in prescribing the infusion was to reduce the heart action as much as possible then the alcohol was acting as an antidote to the drug. If the statements made to the Section were based on fact, the attention of the Revision Committee should be called to the subject before the formula is placed in the next Pharmacopœia.

PROF. J. P. REMINGTON said that we do not know certainly to what digitalis owes its peculiar virtues and until we have a good method of assaying and determining the value of the drug there would be discordant results. If the pharmacist is sure he has obtained a good quality of digitalis does not give it a chance to deteriorate, and makes the infusion freshly and in small quantities, he has done the best he can do under the circumstances.

The conditions which contribute to the deterioration of digitalis are not known exactly. He did not have faith in the putting of digitalis in blue bottles, but preferred a non-transparent container, as a tin can, with a lid not too tight. Frequently leaves are injured by keeping in a tight container which does not permit the evaporation of natural moisture. Until it is known with certainty what the active principles of digitalis are, and their nature, the pharmacist cannot intelligently make its preparations. The best that can be done under the circumstances is to make a preparation which shall contain all of the active principles. He thought that physicians did not generally make any differentiation between the use of digitalis for heart action and for diuretic action. He believed that there are too many alcoholic preparations used and that the use of a greater number of infusions made directly from the drug would be an improvement over the present practice.

Referring to the idea that the value of a drug necessarily indicated its quality, he said that this was not necessarily true. Prof. Kraemer had found that the dark and wormy portion of rhubarb, commonly required to be rejected, is in some cases the most valuable.

Another important question in pharmacopœial work was, how much of the stems of vegetable drugs should be included? The collector of drugs sought to include as much as possible of adherent and extraneous matter, and the importer naturally sought to pass this material on to his customers. In the next revision of the Pharmacopœia it would be endeavored to limit

as much as possible inert portions. In reply to a question as to the reason why the Revision Committee included alcohol in the infusion, he stated that it was for its preservative properties.

MR. HYNSON moved that the papers be referred to the Publication Committee with the understanding that the authors should eliminate all therapeutic references, which motion was seconded by Mr. Wilbert.

MR. FORD referred to the large use of digitalis in Colorado on account of the high latitude and pulmonary troubles. A drug could not be discussed even commercially without therapeutic references. It was desired to give the physician what he expected to get and as digitalis was a drug whose constituents were not well understood, it should be endeavored to give a uniform infusion from the best drug obtainable. He had never been guilty of putting alcohol in the infusion, and had always considered it one of the jokes of the Pharmacopœia.

DR. J. M. GOOD did not see exactly how the authors could be required to eliminate all therapeutic references. He thought the preparation of a drug so as to develop one or another particular therapeutic quality was a very important part of its pharmacy and was properly included in the discussion of such drugs and their preparations.

MR. HOWELL stated that he was prepared to defend his use of therapeutic terms if challenged. The experimental work referred to had been performed in his department and results had been published and read before the American Medical Association.

MR. VANDERKLEED did not think it necessary to eliminate all therapeutic terms, but if Mr. Lascoff would eliminate the statement that physicians wanted to leave out all heart stimulating properties it would be sufficient. Physicians certainly do prescribe the infusion for its diuretic action.

The amendment was accepted and the amended motion was unanimously carried.

MR. HYNSON moved that it be the sense of the Section that pharmacists should be warned against the use of any except infusion of digitalis freshly made, in strict accordance with the Pharmacopœia.

After some discussion, the motion was put to a vote and carried.

ANOTHER VIEW OF PARCELS-POST.

About the only associations now opposed to a parcels-post are those of druggists, while a great many organizations, including the Manufacturing Perfumers' Association, are urging the adoption of the idea. Residents of England, Germany and other foreign countries now have the *privilege of using our mails in this way*, by international agreement, and the equal right to enjoy this service should no longer be denied to the American citizens and taxpayers who "pay the freight" in the form of taxes. All of the arguments against a parcels-post have been exploded by the experience of countries where the system is in operation. President Taft, ex-President Roosevelt, the Postmaster General and leading publicists, as well as prominent business men, all are advocates of the idea, and the only difficulty in Congress seems to be rather one of ways and means than of disapproval of the plan as an economic and desirable feature of our postal service.

With a parcels-post there is no danger of the small dealers being crushed under the "steam roller," unless they are business derelicts waiting for some excuse to get out of trade. It has not happened in other countries and it will not happen here. In fact, the small dealers in the small towns will enjoy more advantages than at present under a parcels-post system.—*The American Perfumer*.