

B	1	92.04	92.60	91.52	73.80	Tin can
B	2	96.44	96.44	97.17	92.20	Tin can
C ²	1	94.74	93.91	92.61	91.84	Paper
D	1	84.70	84.70	84.28	82.54	Paper
F	1	...	94.22	93.00	91.50	Tin can
F	2	92.33	91.76	91.05	90.38	Tin can
F	4	92.50	91.84	91.34	90.67	Glass
G	1	...	86.27	86.36	86.08	Glass

¹ Sample A, 6, was originally a crystalline sulphite purchased in a tin can. In May 1916, it was still in good physical condition but had lost about 12.50 per cent. In 1916 a part of the sample was placed in a glass-stoppered bottle, the remainder left in the original can. The assay given above is for the *crystals placed in the bottle*, and shows almost entire loss of sulphite. Strange as it may seem the sample remaining in the can assayed in 1935 59.00 per cent sulphite. On careful inspection this sample was a fine powder, no crystals whatever. The high content of sulphite is no doubt due to the fact that the can was not air tight and the crystals dried out during the twenty years of storage and this drying process outstripped the deterioration process, thus rendering the remaining portions of the sample more and more stable as the drying went on, the final result being a stable fully dried sulphite. Based upon crystalline sulphite instead of dried, 59.00 per cent would mean about 30 per cent Na_2SO_3 , so the actual loss of sulphite was considerable, aside from the loss of water which is always an economic one.

² Sample C, 1. In 1935 this specimen was found uncovered and very dirty on top, but in spite of this the loss of sulphite was not great.

One may conclude very definitely from the above that a dried sodium sulphite will keep, certainly for three years, probably for five or six years and in some cases as long as twenty years; that crystalline sodium sulphite loses sulphite rapidly, the loss ranging from 12.5 per cent to 100 per cent in two years; that a paper carton or tin can is as safe a container as a glass bottle; that a photographic quality, a U. S. P. quality or an unbranded article is likely to be just as good as an expensive grade.

THE IMPORTANCE OF THE KIDNEYS IN THE STANDARDIZATION OF DIGITALIS.

BY B. BOUCEK.*

The directions in the official publication of the League of Nations for the standardization of digitalis by the method of Hatcher and Brody, as modified by Magnus, require that pregnant cats and those having pneumonia shall not be used for the standardization. It is not explained why such animals are unsuitable, and I have been unable to find elsewhere any statement that any functional or pathological change in any organ influences the result of the test.

It is well known that some individual cats are especially resistant to the toxic action of digitalis. This fact has been confirmed by McFarlane and Masson¹ who state: "Apparently, it represents a separate group of cats which has greater resistance to the toxicity of digitalis and consequently lessens the reliability of this method of assay of the drug unless a large number of animals be done for each estimation."

* Director of the Department of Pharmacology of Masaryk University, Medical School, Brno Uvoz 33, C. S. R., Europe.

¹ McFarlane, A., and Masson, G. A., *J. Pharmacol. and Exper. Therap.*, 30, 293 (1927).

We have observed in rare cases differences of about 50 per cent compared with the average minimum lethal dose; some weak and cachectic animals having manifested great resistance. For example, a twelve-year old cat which had chronic bronchitis, calcifications, emphysema of the lungs, a follicular tumor of the spleen, and fatty degeneration of the liver and kidneys, as shown at the post-mortem examination, required 25 per cent more than the average fatal dose to cause death.

Other animals did not suffer from such a variety of pathological conditions, but in every case where great resistance to digitalis was observed pathological changes were found in the kidneys. Only occasionally was there observed any such influence due to pathological changes in the lungs and liver, or to pregnancy. This is shown in the following table.

Table I shows the effects of pregnancy and pathological changes in organs on the toxicity of digitalis for the cat.

TABLE I.

Resistance.

Lungs	-13 till	-40 per cent
Liver	-40	per cent average
Kidneys	+30	per cent average
Pregnancy	-30 till	-60 per cent

The variation in the lethal dose is slight in healthy animals, not more than about 10 per cent in our experiments. Many of the animals which are delivered to our department are in bad health, most of them being infested with hookworm. This is also true in America. All animals are now treated with a vermifuge, and they are kept under good conditions for some time before they are used for experiments. In every case where an animal shows increased resistance, it is found that the animal had nephritis.

TABLE II.—SHOWS THE EFFECTS OF VARIOUS MEASURES ON THE RESISTANCE OF CATS TO THE TOXIC ACTION OF DIGITALIS.

Treatment.	Number of Animals.	Resistance.	Remarks.
Acute uranium nephritis	11	30% higher	Only one injection of 1.8 to 2.8 mg. $UO_2(NO_3)_2$ per Kg.
Chronic uranium nephritis	5	Without change	$\frac{1}{2}$ cc. solution $UO_2(NO_3)_2$ 1-400 every fifth day
Bilateral nephrectomy	11	18% higher	18-96 hours after nephrectomy
Ligature of blood vessels	3	Without change	Immediately after tying
Ligature in cases of inflammation of the kidneys	1	27% higher	Immediately after tying
Ligature of both ureters	5	Without change
Digitalis with urea	6	20% higher	0.25-1.4 Gm./Kg.
Digitalis with NH_4Cl	6	20% lower	Isotonic concentration with digitalis

This observation led us to determine the resistance of animals to digitalis under the following conditions: (a) In those in which experimental uranium

nephritis had been induced; (*b*) after nephrectomy; (*c*) after tying the renal arteries; (*d*) after tying both ureters. It is interesting to observe that our cats required smaller doses of uranium nitrate than rabbits or guinea pigs.

The tabulated results show that the condition of the kidneys is a very important factor in the determination of the action of digitalis on the heart, and that this factor must not be neglected in the biological standardization of preparations of digitalis.

The immediate cause of the increased resistance to digitalis in the presence of inflammation of the kidneys cannot be determined by the results of the experiments described in this paper.

SUMMARY.

1. The resistance of cats to lethal doses of digitalis is increased by experimentally induced uranium nephritis.
2. Greater resistance to digitalis was observed in cases of inflammation of the kidneys which occurred naturally. This condition is often observed in cats.
3. This increased resistance must be considered, and only those cats which are free from pathological changes in the kidneys must be used in the Hatcher-Magnus method of standardizing digitalis.

EDITOR'S NOTE: We are indebted to Robert A. Hatcher, M.D., of the Department of Pharmacology, Cornell University Medical College, New York, for assistance in the preparation of this paper for publication.

ACTION OF TESTICULAR HORMONE ON THE DEVELOPMENT OF THE HEN'S COMB.*

BY DRS. E. RAMIREZ AND M. D. RIVERO.

Biological control, that is to say, the experimental production of a specific reaction on an animal or on living tissues, permits us to obtain active extracts of endocrine glands, as long as we can rely on a method revealing the activity of the various extracts and the different fractions, solutions and residues, in the sequela of hormone isolation and purification. It has shown, on the other hand, that a large quantity of extracts and ophoterapeutic products, which are prepared regularly for commercial purposes, are completely inactive. Biological control has permitted in some cases to obtain standardization, thus establishing the smallest quantity which could produce a definite and measurable response in certain animals and under some specific conditions.

The specificity of a reaction must be considered as provisional, inasmuch as another product or definite substance, altogether different from the first, may determine a similar action. This happens, for instance, in the horn-shape reaction of the rodent's vaginal epithelium, which is induced not only by folliculin, but also by testicular extracts (Lowe, Lange and Spohr) by filtrates of bacterial cultures (Silberstein, Molnar and Engel), by a lipoid isolated from the Koch bacillus (Padersen-

* Department of Pharmacology, Faculty of Medicine, National University of Mexico, Mexico, D. F.