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THE REPUTED INFLUENCE OF ULTRAVIOLET LIGHT ON THE YIELD OF DIGITALIS GLUCOSIDES.*

BY C. S. LEONARD AND JOHN M. ARTHUR.

It has been claimed that the yield of active drug substances in certain drug plants can be altered by differences in the quality of the light under which they are grown. Thus, McCrea (1) has claimed that if seedlings of *Digitalis purpurea* are sprouted and grown for a time under a glass having a high ultraviolet transmission, then set into the field, dried powdered leaf made from these seedlings will yield more cardiac glucosides, as tested by bioassay than will that from similar plants sprouted under window glass and set out into the field.

In examining this work it appeared to the writers that a number of factors were not controlled in Miss McCrea's experiments and that some of these factors could be kept constant during the experimental period with the facilities available at the Boyce-Thompson Institute. The experiments here reported have been in progress for three years. Two strains of seed of *Digitalis purpurea* were obtained, one from Professor Edward Kremers of the University of Wisconsin and grown at the Pharmaceutical Experiment Station there, the other was obtained from a local seedman of the New York district (called Vaughan's strain). Both species were germinated and grown under the standard conditions possible in two air-conditioned greenhouses of the Boyce-Thompson Institute, but one group of each was under "Sunlit" glass with which one greenhouse is glazed, the other under ordinary window glass. The "Sunlit" glass used varied in thickness from 2.5 to 3 mm. Coblentz and Stair (2) found an average transmission for "Sunlit" glass at wave-length 302 mμ of 65% when new and 39% after solarization by exposure to a mercury vapor

* Contribution from the Burroughs Wellcome and Company Experimental Research Laboratories, Tuckahoe, N. Y., and from the Boyce-Thompson Institute for Plant Research, Inc., Yonkers, N. Y.

arc. The average thickness of the samples tested was 2.3 mm. Similarly, the figures determined for "Vita" glass for like wave-length and thickness were 48% and 22%, respectively. Coblentz and Stair have pointed out that a variation in thickness of 0.1 mm. produced a change in transmission of 1.2% at a wave-length of 302 mμ. The limit of transmission of the window glass is 313 mμ. No difference of morphology of the plants (size, etc.) has been seen.

I. EXPERIMENTS IN WHICH THE PLANTS WERE KEPT FOR THREE TO FOUR MONTHS AFTER GERMINATION IN THE EXPERIMENTAL GREENHOUSES AND WERE NOT SET INTO THE OPEN.

One strain was started July 29, 1930 (Vaughan's), the other in September (Wisconsin), hence the two sets of plants were not of identical age at the time of sampling. On January 12, 1931, six sturdy plants were selected at random from each group for each powder, two powders being made from each group. All but one were dried under the same conditions in the attic of the Boyce-Thompson Institute. One was dried in an electric oven at about 45° C. Eight powders and tinctures were made by the U. S. P. method.[1] A table below gives the results.

TABLE I.—REPORT OF ASSAY BY THE U. S. P. ONE-HOUR FROG METHOD OF TINCTURES MADE FROM DIGITALIS LEAF FROM PLANTS 4–6 MONTHS IN THE GREENHOUSE.

Tincture Number.	Per Cent U. S. P.	Total Solids, Gm. per 100 cc.	Variety.	Greenhouse.	Age, Months.
1	126 ± 10*	4.06	Wisconsin	Window glass	4
2	120 ± 10*	4.11	Wisconsin	Window glass	4
3	200 ± 10*	3.26	Vaughan	Window glass	6
4	150 ± 10*	3.17	Vaughan	Window glass	6
5	109 ± 10*	3.75	Wisconsin	"Sunlit" glass	4
6	150 ± 10*	3.78	Wisconsin	"Sunlit" glass	4
7	150 ± 10*	3.08	Vaughan	"Sunlit" glass	6
8	133 ± 10*	3.20	Vaughan	"Sunlit" glass	6

* Probable error in U. S. P. bioassay (A. O. A. C.).

Comments on Table I.—Three Wisconsin samples were low in bioassay, one high. Three Vaughan samples were high in bioassay, one low. The average for the Vaughan samples is higher than the Wisconsin samples but the plants are several months older so this is to be expected. The average bioassay for the samples from both sources grown under window glass (149%) is higher than that for those grown under the "Sunlit" glass (135%). Hence, any conclusion from this would be that the extreme ultraviolet region is detrimental to the yield of alkaloids. However, as the error of bioassay is ±10%, and there is an additional slight error due to possible variations of extraction, and to the individual variations, which despite the presence of six plants in each powder, were likely to be evident, we believe that the difference seen, namely, 14% U. S. P., is within the possible error of the experiment.

II. EXPERIMENTS IN WHICH THE PLANTS WERE GROWN 4 MONTHS IN THE GREENHOUSES AND SET OUT INTO THE FIELD FOR 5 MONTHS.

The Wisconsin strain only was used. The seed was planted in January. These plants were kept in the greenhouses under the same conditions as in the first experiment. On removal to the open field a part were put into a plot of ground at the Boyce-Thompson Institute, a part at another plot located at the U. S. A.

[1] Type Process P of the U. S. P. X without the modification for the adjustment to U. S. P. strength of assayed tinctures, but rather making directly to 1000 cc.

Works of Burroughs Wellcome & Co., Inc., both in Yonkers, N. Y. A set of six sturdy plants was taken from each field and each group (previously under ordinary glass and previously under "Sunlit" glass). They were dried by spreading on a paper in an attic as before. Four powders and tinctures were made by the U. S. P. method and assayed by the U. S. P. one-hour frog method. The results are given in Table II.

TABLE II.

Tincture Number.	Per Cent U. S. P.	Total Solids, Gm. per 100 cc.	Field.	Greenhouse.	Age, Months.
9	140 ± 10	2.20	B. W. & Co.	Window glass	9
10	84	2.34	B. W. & Co.	"Sunlit" glass	9
11	84	2.70	Boyce-Thompson	Window glass	9
12	70	2.24	Boyce-Thompson	"Sunlit" glass	9

Comments on Table II.—The results tend to be lower than in the previous test, apparently because of the time of sampling. Those specimens originally under window glass were up to 70% U. S. P. higher in potency by bioassay than specimens otherwise of similar history, but originally under "Sunlit" glass. In different fields the variation in specimens of identical history is evident. This variation is from 14% to 56% U. S. P. The evidence thus afforded that the glucoside yield varies enormously with soil conditions seems significant.

III. EXPERIMENTS IN WHICH THE PLANTS WERE GROWN 9 MONTHS IN THE GREENHOUSE AND NOT SET INTO THE FIELD.

A portion of the seedlings of Experiment II were not set out into the field but were continued for the nine months in the air-conditioned greenhouses. Two sets of 6 sturdy plants were taken from each group. They were dried as before. Four powders and tinctures were made by the U. S. P. method and assayed by the U. S. P. one-hour frog method. The results are given in Table III.

TABLE III.

Tincture Number.	Per Cent U. S. P.	Total Solids, Gm. per 100 cc.	Greenhouse.	Age, Months.
13	60 ± 10	3.40	Window glass	9
14	84	3.34	Window glass	9
15	112	3.22	"Sunlit" glass	9
16	76	2.96	"Sunlit" glass	9

Comments on Table III.—The specimens grown throughout in the greenhouse also show considerable variability although here set in the same soil and kept under the same conditions as regards all factors but light. The difference in the same greenhouse of two specimens is 36% U. S. P. in the case of the specimens under "Sunlit" glass and 24% in the case of the ordinary glass. The average of the former is 94%, the average of the latter is 72%. Thus, here the specimens under "Sunlit" glass are higher in glucoside yield by 22% U. S. P. if the averages are compared, but the differences between specimens of identical history is greater (24–36% U. S. P.) and if the 84% specimen from the greenhouse with ordinary glass were compared with the 76% specimen from the house with "Sunlit" glass, the former would appear to have the advantage.

IV. EXPERIMENTS IN WHICH THE PLANTS WERE GROWN IN THE GREENHOUSES FOR 8 MONTHS, SET INTO THE FIELD OVER THE WINTER AND HARVESTED JUST BEFORE FLOWERING TIME.

As the plants grown in the previous experiments had no cold dormant period, they failed to send up flower stalks and flower. The objection might be raised that

these plants were abnormal because they did not flower. The time specified in the pharmacopœias for harvest of digitalis is just before the flowering time. Seedlings of the Wisconsin strain were grown therefore in the greenhouse for 8 months. They were germinated in January, repotted once and set out in October into two fields, one at the Boyce-Thompson Institute experimental ground and the other at the Works of Burroughs Wellcome and Company. After the usual winter dormant period of these perennials, many plants produced abundant and vigorous foliage the following spring and sent up the usual flower stalk in May. They were harvested May 27th, over 17 months after germination and after 8 months of life in the greenhouses and 9 months in the field. Six specimens were collected, 2 sets of 6 sturdy plants from the Boyce-Thompson plants of each group and one set from each group grown at the Burroughs Wellcome field. The results are given in Table IV.

TABLE IV.

Tincture Number.	Per Cent U. S. P.	Total Solids, Gm. per 100 cc.	Field.	Greenhouse.
17	104 ± 10	2.20	Boyce-Thompson	Window glass
18	74	2.27	Boyce-Thompson	"Sunlit" glass
19	61	2.20	Boyce-Thompson	Window glass
20	95	2.36	Boyce-Thompson	"Sunlit" glass
21	87	2.43	B. W. & Co.	Window glass
22	77	2.44	B. W. & Co.	"Sunlit" glass

A specimen from plants similarly treated except grown under window glass of unknown light transmitting power gave a potency of 114% U. S. P.

Comment on Table IV.—It is evident from comparing this group to Group I that the yield of active glucosides is greater in dried powdered leaf from young plants, 6 months of age, than from older plants whether these are about to flower or not. The young plants display average yields nearly double that of the older. This agrees with the observation of Miss McCrea (3). For the plants of pharmacopœial standard age (flowering time) the average of the specimens under window glass is 84%, that of the specimens under "Sunlit" glass is 82%. The difference is negligible, far within the error of the experiment.

DISCUSSION.

Finally, we may average and compare all the results of each type obtained in the four experiments on the total of 22 specimen tinctures made from the specimens, 11 with a history at least as seedlings of growth with no ultraviolet light, 11 supplied with ultraviolet light. The specimens under window glass average 110.4%, the specimens under "Sunlit" glass average 102%. This difference is about 8% U. S. P. and is well within the error of bioassay and hence it is not believed that the difference is significant, particularly in view of the wider variations which are to be seen in specimens of identical history. For example, specimens 17 and 19 are two lots of the same sort of specimens. They show 33% U. S. P. difference. Numbers 15 and 16 similarly are comparable and show 36% U. S. P. difference. Only in the experiments of Group III were the specimens under "Sunlit" glass higher than the specimens under window glass and then less than the above 36%. No consistent, significant differences were found in yield of glucosides as were found by McCrea. The above experiments demonstrate the great variation in glucoside yield which can be seen in sets of plants of identical prior history set into different fields or even from different regions of the same field. Even when

grown in pots, with a presumably uniform soil and kept under controlled and constant greenhouse conditions, two lots of 6 plants each, both under "Sunlit" glass, show as much as 36% U. S. P. variation. The averages obtained in the experiments here reported do not permit any assumption that the influence of the extreme ultraviolet region of sunlight, either during the seedling stage or throughout the life of the plant, affects the yield of active glucosides.

SUMMARY.

No significant differences in glucoside yield could be observed between digitalis plants grown under a glass having a higher ultraviolet transmission and those grown under ordinary window glass, whether the plants were kept until sampled in the air-conditioned greenhouses or were set out after some months of such treatment into the open field.

Digitalis plants were found to require a cold dormant period in order to induce flower stalk formation. Miller (4) and Thompson (5) have reported a similar cold period requirement for the flowering of two other biennials, celery and cabbage.

Dried powdered leaf from young plants 4 to 6 months old has nearly double the glucoside content of that from older plants (9–17 months old) whether a flower stalk is formed on the older plants or not.

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STUDY OF GERMICIDAL AND ANTISEPTIC ACTIVITIES OF SOME DERIVATIVES OF 8-HYDROXY QUINOLINE.*

BY E. MONESS AND W. G. CHRISTIANSEN.

8-Hydroxy quinoline has bacteriostatic properties and is generally used in the form of its sulphate, which is water soluble. Matzumura (1) prepared 5-8-dihydroxy quinoline, and the presence of the additional hydroxyl suggested the possibility that such a compound may be soluble in an aqueous medium without resorting to salt formation.

This compound was prepared, as well as two chlorinated derivatives of it, and all were found to be soluble in a vehicle containing 30 parts of alcohol, 40 parts of

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