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Occurrence of Antigoitrogenic Substances in Plant Juices.

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The discovery by Chesney, Clawson and Webster^{1, 2, 3} that cabbage when fed to rabbits as their principal food produces marked thyroid hyperplasia has provided a rapid and more practical method for testing various antigoitrogenic agents. Last year we showed that cabbage grown in the spring and early summer is much less goitrogenic than cabbage maturing in the late autumn.⁴ Also it was pointed out that whole press juice and juice concentrates made from potent goiter-producing cabbage had little or no goitrogenic activity.

Further work showed that the goitrogenic activity of cabbage was in general inversely proportional to its ability to absorb iodine. This suggested that there were 2 substances in cabbage in variable amounts, one of which was goitrogenic and the other antigoitrogenic. This view is further supported by the fact that washing hashed, steamed cabbage with water increases its goitrogenic activity. Since the antigoitrogenic activity corresponds roughly to the amount of reducing substance (determined iodometrically), we have sought an available plant which contained the reducing substance in greater amounts than is ordinarily found in common vegetables. We have obtained very potent concentrates from the juice of skunk cabbage (*Symplocarpus foetidus*) and have found that it produces thyroid involution in rabbits in from 8 to 10 days when fed by mouth daily in amounts equivalent to 100 units (a unit being the amount of juice required to absorb one cc. of N/100 iodine) in addition to our standard stock diet of oats and alfalfa hay. Sterile fractions introduced intraperitoneally appear to be more effective. Fresh cut alfalfa and lawn grass also produce involution of thyroid hyperplasia when fed to rabbits in amounts of 300 to 400 gm. daily for 3 weeks. The early spring growth of all of these plants contains large amounts of the iodine-absorbing material. Plant juices which are extremely low in the reducing substance have little or no

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¹ Chesney, A. M., Clawson, T. A., and Webster, B., *Johns Hopkins Hosp. Bull.*, 1928, xliii, 261.

² Webster, B., Clawson, T. A., and Chesney, A. M., *Johns Hopkins Hosp. Bull.*, 1928, xliii, 278.

³ Webster, B., and Chesney, A. M., *Johns Hopkins Hosp. Bull.*, 1928, xliii, 291.

⁴ Marine, D., Baumann, E. J., and Cipra, A., *Proc. Soc. Exp. Biol. and Med.*, 1929, xxvi, 822.

antigoitrogenic action. This antigoitrogenic substance is present in a great variety of plants but in highly variable amounts as regards age, species and climate.

Whether this reducing substance is identical with that which Szent-Györgyi⁵ isolated from cabbage, orange juice and suprarenal cortex and found to be a hexuronic acid has not been established. All the evidence at present indicates that this reducing substance is at least one of the substances causing thyroid involution. The facts that a similar reducing substance occurs in the suprarenal cortex, the corpus luteum and the gonads and that we⁶ have demonstrated that extracts of the suprarenal cortex have an inhibiting or regulatory effect on thyroid activity also support the view that the reducing substances in plants which involute thyroid hyperplasia belong to the same group of compounds which Szent-Györgyi isolated from the suprarenal. There is also evidence that this reducing substance hastens thymus involution and increases the weight of the suprarenals in rabbits. The involuting effect of these reducing substances is not due to iodine.

The iodine content of sheep, beef and hog thyroids as shown by Seidell and Fenger⁷ is lowest in the early spring months. On the other hand the incidence of goiter in animals is highest during this season of the year when the amount of reducing substances in stored foods is at its lowest level. As the animals obtain fresh green food, the iodine content of the thyroid rises. Up to the present this rise in the iodine store has been assumed to be dependent upon an increased intake of iodine, but from the observations we have made it appears probable that the iodine store rises because the thyroid hormone is less needed. The relation of the suprarenal glands and gonads to thyroid enlargement also becomes more understandable in the light of these experiments. The suprarenals and gonads are normally a storehouse and possibly a place of manufacture of the reducing substance and so long as the supply of reducing substance is available in ample quantities it exerts a sparing action on the thyroid. We have repeatedly pointed out, in discussing the relation of iodine to thyroid enlargement,⁸ that one must recognize those enlargements dependent upon an absolute deficiency of iodine (endemic goiter) and those dependent upon a relative deficiency (sporadic goiter), that is, due to conditions which increase the needs of the body for iodine as occurs in the thyroid enlargement of puberty,

⁵ Szent-Györgyi, A., *Biochem. J.*, 1928, xxii, 1386.

⁶ Marine, D., Baumann, E. J., and Cipra, A., *Am. J. Physiol.*, 1925, lxxii, 248.

⁷ Seidell, A., and Fenger, F., *J. Biol. Chem.*, 1913, xiii, 517.

⁸ Marine, D., *Medicine*, 1927, vi, 127.

pregnancy, Graves' disease and other associations. One of the conditions producing the relative iodine insufficiency now appears to be a deficiency in the reducing substance.

It is our present belief that plant juices prevent or cure thyroid hyperplasia by a thyroid-sparing acting, that is, by providing another mechanism for promoting tissue oxidations. On the other hand, iodine administration prevents thyroid hyperplasia by making it easier for the thyroid to produce more thyroxin.

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Action of X-rays on Glutathione Content and Oxygen Consumption of Normal and Regenerating Planarians.*

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Studies upon regeneration¹ have been carried out to test the hypothesis that persistent embryonic cells are responsible for the formation of new tissues during regeneration, and that the power or capacity for regeneration is to be correlated with the number of such cells present. It has been shown that in different species of planaria, cells of an embryonic type, called "formative cells," undergo rapid proliferation after cutting the planarian, migrate to injured areas, and differentiate into the new tissues characteristic of the regenerating part. Species of planarians that exhibit the greatest capacities for regeneration possess the greatest numbers of these formative cells. Hickman² destroyed the capacity for regeneration by the use of X-rays and radium, and histological studies of such irradiated worms showed a selective destruction of these formative cells.

Other investigators showed that the rate of metabolism and of oxygen consumption in particular, increase immediately after cutting and remain at a high level throughout regeneration. The important rôle of glutathione in the establishment of the metabolic level and in the utilization of oxygen indicated that important cor-

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¹ Curtis, W. C., *Proc. Boston Soc. Nat. Hist.*, 1902, xxx, 515.

² Curtis, W. C., and Hickman, J. F., *Anat. Rec.*, 1926, xxxiv, 145.