

both stress and the catabolic action of fludrocortisone to withstand.

Since cortisone enhances the renal damage caused by DCA(6), the great augmentation of renal enlargement and renal pathology by stress in rats receiving large doses of that steroid(2) could be construed as indicating that stress caused the adrenals to secrete a cortisone-like glucocorticoid. The present experiment seems to weaken the force of this hypothesis since stress did not as dramatically enhance the nephrotoxic action of fludrocortisone, which possesses both mineralocorticoid and glucocorticoid activity in high degree. It must be emphasized however, that stress enhances the pathologic effects of DCA on the vasculature much more markedly at high dosage of hormone than at low(2), and perhaps the results might have been more striking had a higher dosage of fludrocortisone been employed. The finding of either interstitial nephritis or fibrosis in 3 of the stressed animals is interesting. Such lesions were absent from controls, and animals receiving only steroid. Seemingly therefore the lesions were not of natural occurrence in the strain and may have been caused by stress, but suppressed by the anti-inflammatory effect of fludrocortisone in the steroid-treated stressed group. The slight incidence, however, precluded definite conclusions as to etiology and pathogenesis.

Summary. The influence of stress upon

the response to fludrocortisone was assessed. The steroid caused atrophy of the spleen and thymus and hypertrophy of the heart and kidney, changes which were neither induced nor modified by stress. Body growth was slightly retarded by stress and markedly impaired by fludrocortisone, but the effect of combined treatment was greatest. Although the steroid alone caused adrenal involution, adrenal hypertrophy was found in animals subjected to stress or to stress and steroid treatment together. Mortality was insignificant from steroid alone, but great among animals subjected also to stress. There was some indication that stress enhanced the hypertensive and nephropathic response to steroid treatment, but precise assessment of this effect was rendered difficult by high mortality in the group exposed to dual treatment and the prevalence of emaciation and lowered vitality among survivors.

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Antithyroid Effect of Barbarin (Phenylthiooxazolidone), A Naturally-Occurring Compound from *Barbarea*.* (26760)

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The capacity of certain crucifers to produce goiter has been known for some time (1). A potent antithyroid compound, goitrin (vinylthiooxazolidone), has been isolated from the edible parts of some members of this family(2,3,4,11) but seems to be contained in significant concentration only in

turnip and rutabaga. It is present as an inactive thioglycoside, progoin(5), from which goitrin is released by enzymatic hydrolysis. Goitrin has an antithyroid potency 33% greater than propylthiouracil (PTU) in man and 2% that of PTU in the rat(2).

Recently a related compound, barbarin (phenylthiooxazolidone), has been isolated

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TABLE I. Antithyroid Activity of Barbarin in Rats.

Test material	Dose, mg	No. of animals	Avg % uptake
Barbarin	10	2	10.4
"	25	2	8.3
"	50	2	5.5
PTU	0.2	1	8.3
"	1.0	2	3.9
Control*	—	2	18.5

* Vehicle only.

from various species of *Barbarea* and from *Reseda luteola*(6,7). This material is contained in quite high concentration as its thioglycoside, glucobarbarin, in the edible green parts of the plants, which have heavy and widespread distribution through northern Europe. They are consumed by livestock and in some areas the young plants are eaten in salads or as vegetables. For this reason it was considered of interest to determine the antithyroid activity of barbarin.

Materials and methods. Because of the small amount of barbarin available, only limited studies could be made. Holtzman rats weighing 250 g were fed a low-iodine diet for 7 days. They were then injected subcutaneously with the test substance suspended in 10% gum acacia in saline. One hour later, 0.1 μC I^{131} was injected intraperitoneally. The thyroids were removed and counted in a scintillation well-counter 4 hours after radioiodine administration.

Assays in man were made by the technic of Stanley and Astwood(8). Epithyroidal counts were made at intervals of 20 minutes following administration of a tracer dose of

10-20 μC I^{131} and thyroidal radioactivity plotted as percent of the administered dose against the square root of the time in minutes. Once the slope of the "accumulation gradient" thus obtained had become clear (usually approximately 2 hours), the indicated dose of test substance was administered orally. Counting was continued at 20 to 60 minute intervals for the next 6 to 7 hours and repeated again 24 hours after the initial radioiodine administration. Changes produced in the accumulation gradient were graded from 0 (no effect) to 5 (maximal suppression) according to the classification of Stanley and Astwood. In addition, the 24-hour uptake calculated from the accumulation gradient was compared with the actual 24-hour count(9).

Results and discussion. The results are summarized in Tables I and II. Barbarin had an antithyroid activity roughly 1% that of PTU in the rat. The antithyroid effect of barbarin in man was about 75-100% that of PTU. Only limited examination was made of PTU since this had been extensively studied by Stanley and Astwood(8). Our previous assays of this drug as well as in the present investigation have confirmed their results.

This study indicates that barbarin has a significant antithyroid action, as would be expected from its structure. In both man and rat it is approximately 50% as potent as goitrin. The consumption of considerable quantities of plants containing this compound might therefore be a factor leading to development of goiter in both man and ani-

TABLE II. Antithyroid Activity of Barbarin in Man.

Subject	Drug	Dose (mg)	Effect	Accumulation gradient		24-hr uptake (%)	
				Initial	After drug	Predicted(9)	Actual
Mi	Barbarin	10	0	.69	.69	20.0 \pm 3.2*	22.4
Mo	"	25	0	.84	.84	23.9 \pm 3.7	26.1
Be	"	50	4	.97	.00	27.2 \pm 2.7	18.9
Je	"	50	2	1.65	.40	42.6 \pm 3.1	22.2
Wo	"	100	2	1.77	.18	45.1 \pm 4.8	33.9
Lo	"	100	0	.93	.93	26.2 \pm 3.5	24.7
Mi	"	200	4	.78	.06	22.4 \pm 2.3	16.1
Na	"	283	4	.74	.00	21.3 \pm 2.0	14.5
Je	PTU	50	2	2.34	.32	55.1 \pm 5.4	38.5
Sa	"	100	3	.90	.00	25.4 \pm 2.3	16.1

* Mean \pm S.D.

mals. The activity of barbarin in animals which might feed vigorously on the wild plant is unknown. It is unlikely, however, that enough barbarin would be transmitted to cow's milk to be a potential hazard in the human consumption of this milk(10).

Summary. The antithyroid potency of barbarin, a phenylthiooxazolidone obtained from various species of *Barbarea* and *Reseda luteola*, was assayed by its inhibition of radioiodine uptake in rat and man. In both species it was found to be approximately 50% as active as goitrin (vinylthiooxazolidone).

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Cytopathogenicity of Mumps Virus in Cultures of Chick Embryo and Human Amnion Cells.* (26761)

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Primary monolayer cultures of chick embryo (CE) and human amnion (HA) cells have been utilized in assay of a number of animal viruses. To our knowledge, cytopathogenicity of mumps virus for these cells has not been previously reported. In the present paper cytopathic changes are described which were induced in these systems by mumps virus.

Methods and materials. Cell cultures. Methods of preparation and maintenance of primary cultures of HA and CE cells have been described(1,2). HA cells were maintained on Enders' medium(1) and CE cells on a medium consisting of 2.5% heat inactivated calf serum, 1.5% chick embryo extract, 48% bovine amniotic fluid (BAF), and 48% Hanks' Balanced Salt Solution (BSS). For plaque assay 3% Difco agar in BSS was

added to an equal volume of a solution of 10% inactivated calf serum and 90% BAF. Neutral red dye (final concentration 1:20,000 or 1:40,000) was added 5-7 days after inoculation of virus. Dilutions of virus were incubated with cells for two hours at 37°C prior to overlay with agar. **Virus.** Two strains of mumps virus were employed: a) Enders strain, passaged 47 times in the amniotic cavity and 6 times in the allantoic cavity of the embryonated egg; b) a strain which caused CPE in HA cells on primary isolation,[‡] and was subsequently passed 8 times in these cells. **Serological tests.** Complement fixation, neutralization and hemagglutination inhibition tests with anti-mumps guinea pig serum[§] and hemadsorption of guinea pig erythrocytes were performed by

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[‡] This was one of several strains of mumps virus isolated in HA cells by Dr. S. Kibrick in this laboratory.

[§] Obtained from Microbiological Associates, Inc., Washington, D.C.