pare the action of antibiotics and thiouracils under identical conditions on the thyroid gland.

A colony of immature white rats, approximately 45 days old, was divided into 5 groups of 4 animals each. The groups received the same basic diet (Pratts Nurishmix with 1% iodized salt). Exclusive of the control, each group received their drug by blending it into the ground food in the following concentrations: aureomycin or potassium penicillin G, 1 mg/kg; iodothiouracil (Itrumil) or propylthiouracil, 2%.[3] The animals were permitted to eat ad libitum for 42 days and were weighed weekly. A dose of 20 μc I^{131} was injected iv into these animals exactly 48 hours before the conclusion of this experiment. Following this, the rats were sacrificed, the radioactive count obtained, and the thyroids studied histologically.

It was observed that the thyroid/total body weight ratio as well as the uptake of I^{131} compared favorably (Table 1). All the test groups showed an increase in

TABLE 1.

	Comparative size of thyroid glands (% total body wt. $\times 10^{-6}$), av.	Uptake of I^{131} by thyroids (cpm/mg tissue)	
		Av.	% control
Control	1.94 ± 0.48	543 ± 47	100
Potassium penicillin G	3.73 ± 0.51	149 ± 41	27.4
Aureomycin	7.63 ± 1.03	115 ± 23	21.1
Itrumil	23.5 ± 4.8	0.7 ± 0.2	0.12
Propylthiouracil	41.5 ± 7.9	58 ± 16	10.6

size of the thyroid and a marked depression of the uptake of I^{131}. However, the changes induced by the antibiotics were not as great as by the thiouracils. Histologically, in one of the aureomycin-fed rats, there was evidence of hyperplasia; no changes were observed in the penicillin-fed group. In addition, the vascularity after Itrumil was far less than after propylthiouracil thus confirming the observations of other investigators (*5*).

In our observations, there is suggestive evidence that aureomycin and potassium penicillin G have a goitrogenic action which simulates the thiouracils. It is of major interest to note that it has been suggested that pharmacologically thiouracils disturb uracil metabolism (*6, 7*) and that penicillin disturbs nucleic acid synthesis (*8*). Although limited data have been presented, there is evidence that aureomycin and potassium penicillin G inhibit thyroid activity as measured by the uptake of I^{131} and the weight of this gland.

[3] We wish to thank the Ciba Pharmaceutical Products, Inc., for their generous supply of Itrumil, and Wyeth, Inc., for the potassium penicillin G.

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Production of Triuret from Uric Acid by Ultraviolet Irradiation[1]

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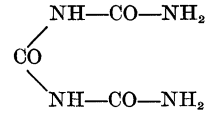
As part of a program involving the relation of the chemical and biological effects of the irradiation of nucleic acid derivatives (*1, 2*), uric acid has been irradiated with ultraviolet light. This paper deals with the production in this manner of triuret, which is not known to be produced under physiological conditions.

Two-liter portions of uric acid solution in water (0.1 mg/ml, pH adjusted to 6.5) were irradiated at room temperature for 2 hr in large white enamel pans by batteries of 7 G.E. germicidal lamps placed about 1 cm above the surface of the solution. The specific ultraviolet absorption spectrum of uric acid had completely disappeared by that time. The solution was concentrated *in vacuo* at 35–40° C and placed in the refrigerator. A yellow crystalline precipitate was formed which was filtered off and recrystallized four times from boiling water. The substance crystallizes in colorless leaflets. It is insoluble in ether and chloroform, sparingly soluble in cold water and ethanol, and soluble in alkalis, acids, and boiling water. It does not show an ultraviolet absorption spectrum. On heating in 1*N* NaOH solution, ammonia is liberated. The substance has the following composition: C, 25.00%; H, 4.09%; N, 38.49%.[3] This checks well for an empirical formula of $C_3H_6N_4O_3$: C, 24.5%; H, 4.1%; N, 38.4%. This and the solubility characteristics suggested to us that the substance might be triuret (1,3-dicarbamylurea):



The melting point of the substance after prolonged drying in high vacuum at 50° C is 237° C when determined in a sealed capillary tube. This is in good accord

[1] Done under terms of contract No. AT(30-1)911 with the Atomic Energy Commission.

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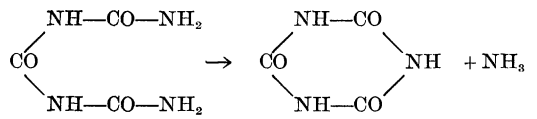
[3] All analyses were carried out by C. Tiedcke, Teaneck, N. J.

with the values of 231–235° reported for triuret (*3, 4*).

When triuret is heated in contact with air or in solution in 1*N* NaOH, it is transformed into cyanuric acid with elimination of ammonia (*5, 6*):

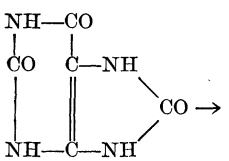


Under both conditions our substance formed cyanuric acid which was identified by the crystalline amethyst-colored precipitate which is formed when a solution of ammoniacal cupric oxide is added to a solution of cyanuric acid (*7, 8*).

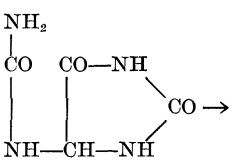
We then prepared a sample of triuret by the method of Schittenhelm (*9*)—oxidation of uric acid in ammoniacal solution by hydrogen peroxide. The three times recrystallized triuret had the following composition: C, 24.55%; H, 4.25%; N, 38.43%; it gave a melting point of 235°. On mixing our substance and this triuret, the same melting point was obtained.

We wanted to characterize our substance further but found that none of the usual amide derivatives had been prepared from triuret. We chose xanthydrol as a reagent because it is frequently used to characterize urea. The directions of Phillips and Pitt (*10*) were followed with the exception that the reaction mixture was heated on the steam bath rather than at 85° C, in order to dissolve the triuret. The product was recrystallized from a dioxane-water (2 : 1) mixture and dried in high vacuum at 50° C (analysis: found C, 68.81%; H, 4.68%; N, 11.01%; calculated for $C_{29}H_{22}O_5N_4$: C, 69.0%; H, 4.4%; N, 11.00%). The melting point was 279° C. The same derivative was prepared from the authentic triuret and showed a melting point of 277° C.

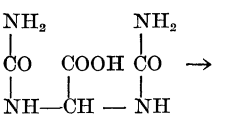
From the preceding results it appears that the substance which has been isolated from irradiated uric acid is triuret. We can only speculate as to the mechanism of its formation and suggest that a possible pathway could be through allantoin to allantoic acid which could be decarboxylated and oxidized to triuret:



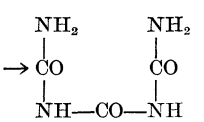
Uric acid



Allantoin



Allantoic acid



Triuret

The yield of triuret corresponds to about 10% of the uric acid; this is a sizable amount in view of the considerable simultaneous formation of ammonia and urea (*2*). We have evidence that other products are being formed in addition to triuret, which we have not yet been able to isolate and characterize except for cyanuric acid, whose presence has been detected in small amounts in the irradiated solution by the above mentioned reaction.

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