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Influence of Ascorbic Acid on Oxidation of Tyrosine by Ultraviolet Light.

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In a previous communication[1] experiments were reported which indicated that there is a close similarity in melanin formation from tyrosine by tyrosinase and by ultraviolet light. The same similarity can be observed concerning the influence of ascorbic acid on this process.

The influence of ascorbic acid on oxidation and oxidation products of tyrosine is threefold. 1. Ascorbic acid markedly furthers dopa formation. It has been shown[2, 3] that in the tyrosine-tyrosinase system more dopa is formed if ascorbic acid is present. 2. Ascorbic acid prevents the further oxidation of dopa. The inhibitory effect of ascorbic acid on oxidation of poly-hydroxy-phenols by any kind of oxidative agent was observed as early as 1930.[4] 3. Melanin is transformed by ascorbic acid into a lighter product called "reduced melanin".[5, 6]

This third effect on melanin is due to the reducing power of ascorbic acid and can be performed with any reducing agent. However, the paradoxical combination of enhancement of tyrosine transformation to dopa and inhibition of further oxidation is a unique effect of ascorbic acid.

When studying the effects of ascorbic acid on oxidation of tyrosine by ultraviolet light the first effect observed was a very marked acceleration and increase of dopa formation. In one experiment the values were 7.2 mg % dopa with ascorbic acid and 2.9 mg % dopa without ascorbic acid after irradiation for 90 minutes. This effect was not simply due to the inhibition of melanin formation with a subsequent accumulation of dopa but it was proven to be a true catalysis of tyrosine oxidation as shown in the correspondingly faster decrease of tyrosine concentration.

After stopping the radiation and keeping the irradiated tyrosine

1 Rothman, S., PROC. SOC. EXP. BIOL. AND MED., 1940, **44**, 485.

2 Schaaf, F., *Helvet. Chim. Acta*, 1935, **18**, 1017.

3 Evans, W. C., and Raper, H. S., *Biochem. J.*, 1937, **31**, 2155.

4 Szent-Györgyi, A., *Science*, 1930, **72**, 125.

5 Figge, F. H. J., PROC. SOC. EXP. BIOL. AND MED., 1939, **43**, 127; *J. Cell. and Comp. Physiol.*, 1940, **15**, 232.

6 Miescher, G., and Minder, H., *Strahlentherapie*, 1939, **66**, 6.

TABLE I.

	Tyrosine irradiated 75 minutes with acetic acid	ascorbic acid
Initial pH	2.8	2.8
Tyrosine mg %	47.8	43.8
Dopa mg %	3.1	7.0

ascorbic acid mixtures in the dark a rapid further increase of dopa concentration occurred. Concerning this effect it must be remembered that the transformation of tyrosine to dopa by ascorbic acid occurs also in the dark without addition of any oxidative agent.[2, 7] However, the dopa formation in the dark after irradiation was considerably faster than in non-irradiated samples. Apparently ascorbic acid acts in this process as a transmitter of atmospheric oxygen and the reaction is markedly accelerated by ultraviolet light. In a relatively short time one-half the amount of tyrosine in a 50 mg % solution could be transformed into dopa by light and ascorbic acid.

Not only tyrosine but any para-mono-hydroxy-phenyl derivative is transformed into the corresponding catechol derivative by ascorbic acid. Thus synephrin is transformed into epinephrine. Highest epinephrine concentrations can be obtained by irradiation of synephrin with ascorbic acid but considerable amounts are also formed if the synephrin-ascorbic acid mixture is kept in the dark for 2-3 weeks. Such a transformation is known to occur also by ultraviolet irradiation alone.[8, 9] However, in this case, the epinephrine formed by ultraviolet light undergoes further oxidation and destruction, so that with light alone it is not possible to produce those high concentrations which are formed in presence of ascorbic acid stabilizing the catechol derivative and preventing further oxidation.

The stabilization of dopa by ascorbic acid and the prevention of further oxidation by irradiation are absolute if an excess of ascorbic acid is constantly present during the exposure to ultraviolet light. These findings indicate that any kind of physiologic or pathologic pigmentation can be prevented by ascorbic acid if its concentration in the tissue is sufficiently high.

The presence of ascorbic acid in the suprarenal medulla may have a double physiologic importance: (1) formation of catechol precursors of epinephrine from phenol compounds of the proteins (phenylalanin, tyrosine) and (2) stabilization of the epinephrine after it is formed in the suprarenal glands.

The effect of ascorbic acid and other reducing agents on melanin

[7] Abderhalden, E., *Fermentforschung*, 1936, **15**, 24.

[8] Ewing, P. L., *J. Lab. and Clin. Science*, 1934, **20**, 16.

[9] Konzett, H., and Weis, W., *Arch. f. exp. Path. und Pharm.*, 1939, **193**, 440.

formed by actinic oxidation of tyrosine is characterized (1) by rapid lightening of the color and (2) by formation of a yellow water-soluble substance from the colloidal particles of melanin. The "melanolysis" proceeds at a more rapid rate as the pH is lowered from 7.4 to 2.0. However, it also occurs at physiological pH's. This change might be of importance in the depigmentation of patients with Addison's disease treated with ascorbic acid.[4] The same effect has been obtained in pieces of skin from Negroes.

Summary. Ascorbic acid furthers the actinic transformation of tyrosine into dopa and that of synephrin into epinephrine but inhibits any further oxidation. It reduces melanin to a water-soluble yellow substance.

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Excretion of Androgens and Estrogens in Males with Mammary Carcinoma.*

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We have investigated the excretion of androgens and estrogens in 2 cases of male mammary carcinoma. The results obtained are recorded in Table I.

TABLE I.
Excretion of Androgens and Estrogens in Patients with Mammary Carcinoma.

Case	Sex	Age	Diagnosis	Androgens in mg of Androsterone per 24 hr			Estrogens in γ of Estrone per 24 hr
P.S.	M	80	Scirrhous Carcinoma	3.4	8.1	3.7	0.8-1.04 for
No. 658182			(Breast)	9.4	5.6	9.9	6 samples
						5.4	
A.A.	M	78	Adeno-Carcinoma	5.1	4.1	8.8	<1.25
No. 667313			(Breast)				<2.5
F.G.	M	75	Control for Age and	6.4	4.7	7.3	
No. 694278			Sex (Ileostomy)	9.2	10.1		
S.W.	M	66	Control for Age and	6.7	10.0		
No. 675993			Sex (Skin Graft)	11.4	7.2		
H.D.	F	45	Scirrhous Carcinoma	4.4	4.1	3.8	2.5-5.0
No. 683167			(Breast)	5.0	4.5	6.2	<5.0
E.K.	F	52	Scirrhous Carcinoma	11.8	10.3		
No. 642071			(Breast)	10.0			
O.H.	F	53	Control for Age and	5.2	6.2	5.4	
No. 686366			Sex (Chronic Cholecystitis)	5.2			

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