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STUDIES OF THE MECHANISM OF ULTRA-VIOLET ERYTHEMA FORMATION

II. The effect of an increased and a reduced serotonin content of experimental animals

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Histamine and serotonin are without doubt important factors in the development of inflammatory processes in the skin, and in recent years a considerable amount of research work has been done on these substances (1, 4, 9). As far as the inflammatory process due to UV radiation is concerned, it seems probable that histamine plays no part in the mechanism of UV erythema formation in the skin (12). On the other hand there are some investigations which point to the possibility that serotonin (5-HT) might be the mediator substance in the formation of UV erythema.

Rowley & Benditt (10) studied the oedematous reaction produced in the skin of rats by the following mast cell-damaging agents: ovomucoid, dextran, compound 48/80 and testis extract. They found that 5-HT and histamine also produced oedema; the oedema produced by the former was the more severe. Neither of these two agents produced mast cell damage. The oedema-producing action of 5-HT could be differentiated from the similar action of histamine by the use of specific antagonists. The oedema produced by the mast cell-damaging agents could be partially inhibited by dibenamine (a 5-HT antagonist) but it could not be diminished by pyrilamine (a histamine antagonist). These observations were consistent with the hypothesis that agents which damage mast cells release both 5-HT and histamine, and that in the rat the oedema associated with mast cell damage is largely mediated by 5-HT.

The action of UV light on the skin of the rat was investigated by Claesson et al. (2). They also studied the effect of compound 48/80 and methotrimeprazine. The erythemal reaction could be decreased with methotrimeprazine. The investigators considered this observation to prove that the mediator substance in the ultra-violet reaction of the skin was a substance to which methotrimeprazine was an inhibitor, e.g. 5-HT.

Cerhová et al. (1) studied the effect of skin inflammation elicited by UV irradiation on the blood content of serotonin. Experiments were performed with albino rabbits. An inflammatory reaction was induced by irradiating a depilated skin area 5×5 cm with an UV lamp from a distance of 50 cm in a single 10-minute dose. They found a significant increase in the blood levels of serotonin. The high serotonin level lasted for 48 hours.

This study was undertaken in order to investigate the erythemal response to ultraviolet radiation in animals in which the content of serotonin was artificially altered. The serotonin level was lowered by subcutaneous reserpine injections (3, 6, 7).

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Raised serotonin levels were obtained in animals by giving doses of extrinsic serotonin or by inducing the formation of intrinsic serotonin with a monoamine oxidase inhibitor (5, 8, 11).

Material and Methods

Full-grown male albino mice were used as experimental animals; the weight of the mice varied from 19 to 23 g. The normal room temperature and lighting conditions of a usual laboratory room prevailed before and throughout the experimental period; however, direct sunlight never reached the animals. The mice were divided into four groups of 54 each. The animals in the first group were injected with 5 mg/kg of reserpine[1] once a day for two days before UV irradiation. The animals in the second group were similarly injected with 100 mg/kg of serotonin.[2] The mice in the third group were injected with 10 mg/kg of beta-phenyl-isopropylhydrazine hydrochloride[3] (PIH or JB-516), a potent and long acting monoamine oxidase inhibitor, once a day for three days before UV irradiation. The fourth group served as control. Each of the four groups were further divided into two subgroups for irradiation with UV-B and UV-C.

The radiation sources for UV-B and UV-C, the irradiation technique, and the examination and recording of the degree (scale from 0 to 5) of the erythema were the same as in earlier experiments (12). The radiation dosage was chosen to cause a suitable degree of erythema of the ear of the mouse. If the experiment caused changes in the mechanism of the erythemal reaction this could be observed in the increase or decrease of the degree of the erythema. The irradiation lasted 10, 11 and 13 seconds for UV-B, and 1, 2 and 3 minutes for UV-C. Each specimen group consisted of nine mice. The average erythema observed was presented.

After administration of reserpine the animals showed the typical signs of reserpine action, e.g. lethargy, enophthalmus and diarrhoea. On the contrary the mice treated with serotonin or PIH showed clear signs of increased motor activity and irritability.

Standard statistical methods were used in the analysis of the data on the degree of erythema. Student's t-test was used for testing the significance between the means of control and experimental animals.

Results

The results are presented in Table I.

The control group showed that the first irradiation dose (10 sec. with UV-B and 1 min. with UV-C) caused, on an average, a very slight erythema in waveband UV-B and a little stronger reaction in waveband UV-C. The strongest irradiation doses caused erythema of about degree 2 (slight erythema) in both wavebands. Thus the choice of the irradiation doses was suitable for observation of the slightest changes (increase or decrease) in the erythema of the experimental series.

As is observed from Table I, there is a tendency that the erythema values in the reserpine group in both wavebands are somewhat lower than in the control group. The values in the serotonin and Catrol groups tend to be slightly higher than in the control series. All these changes, however, are statistically insignificant; the most striking difference found (the difference between animals irradiated for 1 minute in waveband UV-C in control and reserpine groups) is only "almost significant" ($0.05 > P > 0.01$).

Discussion

The results obtained in this investigation indicate that changes in the serotonin content of the experimental animals have no effect on erythema formation. The erythema formation and degree are similar whether the tissues contain serotonin in

[1] Serapasil®, Ciba AG, Basel.
[2] Serotonin-creatininsulfat Monohydrat, Fluka AG, Buchs SG.
[3] Catrol® kindly supplied by Astra AB, Sweden.

Table I. *The results of the investigation*

Group	UV-C		UV-B	
	Irradiation time in min	Degree of erythema Mean ± SE	Irradiation time in sec	Degree of erythema Mean ± SE
Control	1	1.5±0.2	10	1.1±0.2
	2	1.9±0.2	11	1.6±0.2
	3	2.2±0.1	13	2.0±0.2
Reserpine	1	0.9±0.2	10	1.0±0.2
	2	1.6±0.2	11	1.4±0.2
	3	2.0±0.1	13	1.8±0.2
Serotonin	1	1.1±0.2	10	1.1±0.2
	2	2.0±0.2	11	1.6±0.2
	3	2.3±0.3	13	2.3±0.2
Monoamine oxidase inhibitor	1	1.5±0.1	10	1.3±0.2
	2	2.0±0.2	11	1.8±0.2
	3	2.4±0.2	13	2.1±0.2

abundance or only in a decreased amount. This fact is the same for both the short and the long ultra-violet wavebands.

Although the serotonin content of the tissue had no effect on the formation of the erythema, there is evidence that serotonin is in some way connected with the process in the skin after UV irradiation. The investigations of Cerhová et al. (1) showed a significant increase in the blood levels of serotonin and histamine after irradiation of the skin with UV. The mechanism of the liberation of these two amines is, however, unknown. Because the maximum values of serotonin are attained several hours before the highest level of histamine, it is concluded that serotonin can act as liberator of tissue histamine. Their investigations concerning the contents of serotonin and histamine in the skin were also very interesting. When a high increase in histamine was noted, the levels of serotonin did not change at all. These results agree with the observations obtained in the present study. Although there are some changes in the serotonin content of the blood after UV irradiation, it is not the mediator substance in the ultra-violet reaction. It is probably only a secondary product in the erythemal process.

SUMMARY

The possible effect in experimental animals of changes in the serotonin content on the mechanism of ultra-violet erythema formation was examined. The experimental animals were 216 white mice, divided into four groups. The first group was given reserpine, the second serotonin, and the third group Catrol, a monoamine oxidase inhibitor. The fourth group served as control. Half of the mice were exposed to short wavelength ultra-violet radiation (UV-C) and half to long wavelength (UV-B) radiation. Three radiation doses were given.

The external ear of the mouse provided the skin to be investigated. The erythemal reaction was recorded on the basis of defined criteria.

It was observed that no significant differences were observed between the four groups of mice. The results indicate that the formation of ultra-violet erythema is not dependent on the serotonin content of the irradiated animals. This fact was the

same for both short and long ultra-violet wavelengths.

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