THE INDUCTION OF PHOTOCONTACT SENSITIVITY IN GUINEA PIGS WITHOUT UVB RADIATION

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Allergic photocontact sensitization could be induced in guinea pigs with 3,3',4',5-tetrachlorosalicylanilide (TCSA), 3,4',5-tribromosalicylanilide (TBS), and bithionol using pretreatment with sodium lauryl sulfate (SLS) and long-wave ultraviolet (UVA) radiation. Mid-wave ultraviolet below 320 nm (UVB) was not necessary for the induction of sensitization. Combined use of SLS pretreatment with UVA radiation resulted in more effective sensitization than combined UVB and UVA radiation.

Higher sensitization rates to TCSA and TBS were achieved by allowing rest periods between each of 5 2-hr exposures to UVA than by daily 1-hr exposures for 10 consecutive days. The opposite result was obtained with bithionol.

Although UVB has been customarily used in the past for induction of photosensitivity, its role is only to irritate the site of induction.

Although a vast quantity of clinical and experimental data has been accumulated in the past 15 years, many important problems remain unresolved concerning the mechanisms of allergic photocontact dermatitis due to halogenated salicylanilides. The experimental induction of allergic photocontact sensitivity was first reported by Vincent and Borselli in 1966 [1] with 3,3',4',5-tetrachlorosalicylanilide (TCSA). Harber et al [2] used a modification of this method and reported successful sensitization with combined long-wave ultraviolet (UVA) and mid-wave ultraviolet (UVB) radiation. Thereafter, this method has been customarily used for the experimental induction of photosensitivity.

In 1970, Cripps and Enta [3] reported that guinea pigs could be sensitized with TCSA within 1 week using combined UVA and UVB, but no sensitivity occurred with radiation for 16 weeks using only UVA. Although the action spectrum of photocontact dermatitis due to halogenated salicylanilides is in the UVA range, UVB radiation was required for the induction of photocontact sensitivity. The significance or role of the UVB exposure has never been clarified.

Herman and Sams [4] proposed that UVB radiation increased the incidence of induction of photosensitivity, compared with exposure to UVA alone, perhaps due to the cutaneous damage produced by the erythrogenic radiation. Such damage increased percutaneous absorption and stimulated greater accumulation of serum proteins in the skin. Although this explanation seems to be quite reasonable, there has been no confirmatory evidence for this opinion.

More recently, Harber et al [5] stated, "It is of considerable interest that in practically all of these experiments the induction of photoallergy, in contrast to elicitation, required not only long-wave UV radiation, but also erythrogenic (280–320 nm) radiation".

The current investigation was performed to determine why UVB is required for the induction of photosensitization.

MATERIALS AND METHODS

Experimental Animals

Female, albino, Hartley strain guinea pigs, weighing 250 to 300 gm., were used.

Induction of Photosensitivity with Sodium Lauryl Sulfate (SLS) and UVA Radiation

A modification of the maximization test of Kligman [6, 7] was used. The nuchal area of 4 guinea pigs was depilated and a 20% aqueous solution of SLS was applied. Sixty minutes later, a 1% ethanol solution of TCSA was topically applied to the site and immediately afterwards the site was irradiated with four 20-w black lights (Toshiba FL20BLB) emitting 300–420 nm (mainly UVA peaking at 360 nm) at a distance of 15 cm for 60 min. The energy output is 4.8 mw/cm² at this distance. Radiation passed through a pane of window glass 3 mm thick in order to insure that no radiation below 320 nm reached the animals. This procedure, application of chemical and exposure to light, was repeated daily for 10 consecutive days. Another group of 5 animals was treated identically except that the irradiation time to black light was increased to 120 min and the procedure was repeated for a total of 5 exposures at 48-hr intervals.
When thick crusty scales developed at the application site, SLS was applied after removal of the crust. The SLS pretreatments were eliminated if at any time the skin became too inflammed.

Elicitation tests for induced photocontact sensitivity were done 14 days after the last sensitizing exposure. A 0.5% ethanol solution of TCSA (0.05 ml) was applied to the depilated back area, which had received no previous exposure to the photosensitizing substance and light. This area was then irradiated with the black light at a distance of 15 cm for 30 min. The test sites were examined for erythema 24 and 48 hr following irradiation. Pilot studies indicated that 0.5% ethanol solutions of TCSA, 3,4,5-tribromosalicylanilide (TBS), and bithionol were not phototoxic with the amount of light used in this study. The animals which revealed positive reactions were examined for contact sensitization. A 0.5% TCSA solution (0.05 ml) was applied to the depilated lumbar area that had not received the test substance previously. The animals were kept in a dark room and test sites were read 24 and 48 hr after application.

An identical induction and elicitation process was performed on other groups of animals using TBS and bithionol.

**Induction of Photosensitivity with UVB and UVA Radiation**

A 1% solution of TCSA in ethanol was applied to the depilated nuchal area of 5 guinea pigs. Immediately after the application, the site was exposed to the black light and sun lamp (Toshiba FL20E) for 60 min at a distance of 15 cm. Four black-light tubes and one sun-lamp tube were housed in a reflector unit. The window glass was not interposed between lamp and skin. The sun lamp emitted rays between 290 to 370 nm (mainly UVB peaking at 300 nm). The energy output of the sun lamp was 1.0 mw/cm² at a target distance of 15 cm. This procedure was repeated daily for 10 consecutive days.

Two other groups of 5 guinea pigs were also treated by the identical process using a 1% ethanol solution of TBS and bithionol.

Elicitation tests for induced contact and photocontact sensitivity were performed 14 days after the last sensitizing exposure by the procedure described above.

**RESULTS**

The results are summarized in the Table. The combined UVA and UVB radiation induced photocontact sensitivity to TCSA in only 1 guinea pig but contact sensitivity did not result. On the other hand, a higher incidence of photocontact sensitization was achieved by the combined use of SLS pretreatment with UVA radiation. All the animals photosensitized to TCSA developed a strong reaction with eczematous erythema and edema, while the guinea pigs sensitized to TBS and bithionol developed a mild reaction without edema. Mild contact sensitivity was induced in 2 animals which were photosensitized to TCSA with SLS pretreatment and five 2-hr exposures to UVA radiation.

**DISCUSSION**

In the present study, guinea pigs could be photosensitized to all the test materials—TCSA, TBS, and bithionol—without UVB radiation.

Cripps and Enta [3] have stated that guinea pigs could not be sensitized with only UVA radiation. Therefore, in the present investigation, the SLS pretreatments that were used to irritate the skin were based on the hypothesis of Herman and Sams [4] that cutaneous damage increases the incidence of induction of photosensitization. Mizuno has also reported that higher sensitization rates were achieved by sunburn or croton-oil dermatitis.*

Kligman [6] demonstrated that inflammation markedly predisposed to contact sensitization and the enhancement obtained with SLS was usually superior to the other common ways of damaging the skin. Chemical irritation with SLS or dimethylsulfoxide enhanced sensitization more than physical trauma such as UV radiation, freezing, or Scotch tape stripping. Similar results were obtained in guinea pigs [8]. However, Willis and Kligman themselves used physical trauma such as Scotch tape stripping and UVB radiation for the induction of photocontact sensitivity [9-11].

The present results indicate that irritation with SLS was more effective than UVB radiation in photocontact sensitization as well as in contact sensitization. The SLS pretreatment and 2-hr irradiation with UVA for a total of 5 exposures at 48-hr intervals induced photocontact sensitivity to TCSA in all 5 guinea pigs and to TBS in 3 of the 5 guinea pigs. On the other hand, combined UVB and UVA radiation induced photosensitivity to TCSA in only 1 of 5 guinea pigs and none to TBS and bithionol. Harber et al [2] reported that photocontact sensitivity was induced with TCSA in 32 of 65 animals (49.2%) and with TBS in 7 of 21 animals (33.3%) with combined UVB and UVA radiation.

The present results confirm that UVB radiation is not indispensable for the induction of photosensitization to halogenated salicylanilides but is required only to irritate the skin. UVB radiation may be omitted when the skin site of induction is irritated by SLS pretreatment.

**REFERENCES**


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