



# THE IMPACT OF ULTRAVIOLET LIGHT ON HISTAMINE RELEASED BY MAST CELLS

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## ABSTRACT

UV irradiation has different effects on the degranulation of mast cells (MCs), and different irradiation intensities are crucial for histamine MC release. In this study, we explored the action of UVC irradiation (with a wavelength range of 240-280 nm) on the degranulation of MCs. After irradiation, two different histamine releasers, compound 48/80 and compound A23187, were used to stimulate noncytotoxic histamine release from rat peritoneal MCs. These compounds activated histamine release, and UVC-irradiation inhibited this effect. Low UVC doses produced stronger and more complete inhibition of the noncytotoxic histamine release from MCs by compound 48/80, and the release induced by the  $Ca^{2+}$  ionophore A23187 showed the lowest UVC sensitivity. Our results revealed that the specific mechanisms of MC degranulation are sensitive to UVC irradiation. We believe that the power of UV irradiation is important for the amount of histamine released by MCs and that UVC irradiation could have therapeutic implications and serve as a new experimental tool for the analysis of different mechanisms of MC degranulation.

**KEYWORDS:** *ultraviolet light, mast cell, histamine, UVC, immunity*

## INTRODUCTION

Evidence about the effect of ultraviolet light on mast cells (MCs) has led to the conclusion that UVB irradiation inhibits MC degranulation in a noncytotoxic manner (1). In contrast, UVA irradiation is without detectable effects, even though some authors reported that when irradiation is stronger, there can be stimulation of histamine rather than inhibition (2); This shows that different irradiation intensities are crucial for histamine release by MCs.

On the other hand, UVA is an effective therapeutic mean in combination with the alkylating drug 8-methoxy psoralen [PUVA-therapy (3)]. Until now, as far as we know, no data has been published about the activation of ultraviolet light with a wavelength in the range of 240-280 nm (UVC) on MCs. Due to the absorption spectra of proteins, nucleic acids, and oxygen, UVC-induced biological effects are mainly mediated by the generation of sulfur and tyrosine radicals in proteins, thymine dimerization in nucleic acids, and the effects of singlet oxygen (4).

In this study, the first data is reported about the action of UVC-irradiation on the degranulation of MCs. We compared the influence of two different histamine releasers by UVC on MC degranulation. Since the mechanism of mediator release from MCs is only partially understood, the question arises whether UVC-irradiation might represent a new experimental tool for analysing different mechanisms of MC degranulation.

Received: 06 June, 2020  
Accepted: 15 July, 2020

2279-5855 (2020)

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## MATERIALS AND METHODS

The cell suspensions, obtained from the peritoneal cavity of male Wistar rats (200-250 g), contained 3-5% MCs and were used without further purification. Histamine was determined according to fluorometric analysis (5). All experiments were designed as parallel determinations of the sample's total histamine content, spontaneous histamine efflux during the experiment, and chemically induced histamine release. 4-5 parallel determinations from each sample (containing 11,000 MCs) were carried out.

The irradiation source was used as a low-pressure mercury lamp with a nearly monochromatic emission at 254 nm. In order to prevent light absorption by multi-cell layers, which is of great significance at short wavelength ultraviolet irradiation, and to ensure a randomly distributed irradiation of the whole cell surface, the cell suspension (4 ml) was passed (with different flow rates) through a cuvette (diameter 0.5mm) which was located at a distance of 2 cm from the irradiation source. The intensity of the irradiation was measured with the aid of a commercially available set containing a calibrated cesium/antimony photosensitive unit.

Two different substances were used for the stimulation of noncytotoxic histamine release from the MCs immediately after irradiation:

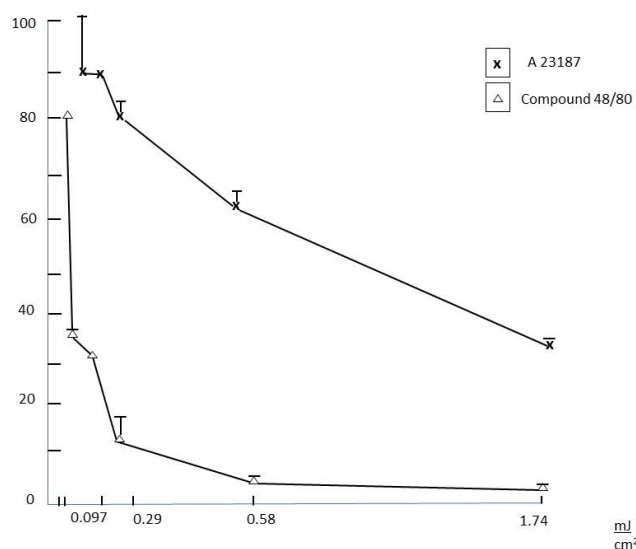
- (a) Compound 48/80, 0.3  $\mu\text{g}/\text{sample}$
- (b) A23187,  $10^{-6}\text{M}$

These concentrations represent optimal values which were derived from the corresponding dose-response curves. The  $\text{Ca}^{2+}$  ionophore A23187 was diluted from a stock solution ( $10^{-4}\text{M}$ ) in dimethyl sulfoxide since it is not directly soluble in aqueous solutions. Control experiments have shown that 1% dimethyl-sulfoxide does not affect the properties of MCs (data not shown).

All data are reported as mean  $\pm$  SD. Statistical calculations were based on the unpaired student's t-test. P values of  $<0.05$  were considered indicative of statistically significant differences.

## RESULTS

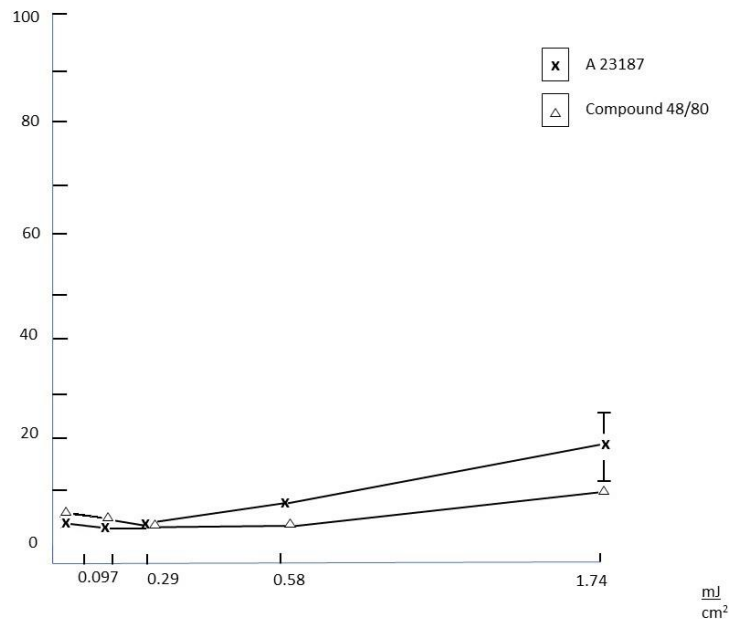
In this study, rat peritoneal MCs were activated by two secretagogues, compound 48/80 at 0.3  $\mu\text{g}/\text{sample}$  and A23187 at  $10^{-6}\text{M}$ , which stimulated histamine release, an effect inhibited by UVC-irradiation. The maximum inhibition was obtained at 1.74  $\text{mJ}/\text{cm}^2$ , while the initial inhibition began at 0.097  $\text{mJ}/\text{cm}^2$  irradiation (Fig.1).



**Fig. 1.** UVC inhibition of two different histamine releasors, A23187 and compound 48/80, on rat peritoneal mast cells (MCs).

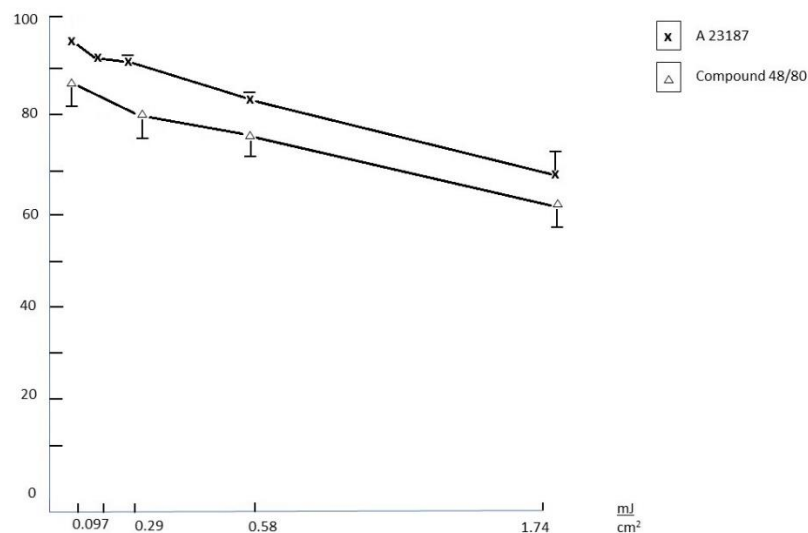
Figure 1 shows that low UVC doses resulted in a strong and complete inhibition of the noncytotoxic histamine release from MCs by compound 48/80. The histamine release that the  $\text{Ca}^{2+}$  ionophore A23187 can induce has the lowest UVC sensitivity, which is documented by the statistical significance of the differences in the effects of UVC irradiation on compound 48/80 induced mediator release.

The UVC-induced effects occur at an irradiation intensity about 1000-fold lower than the UVB, which inhibits the compound 48/80-induced histamine release from rat peritoneal MCs. Contrary to the results obtained with UVB, there is only a slight increase in the spontaneous histamine release at the highest UVC intensities (Fig.2).



**Fig. 2.** Spontaneous histamine release from rat peritoneal MCs after UVC-irradiation in the absence of A23187 and compound 48/80. The data belongs to those cell suspensions used for the histamine release experiments, as shown in Figure 1.

As shown in Figure 3, UVC slightly reduces the total amount of detectable histamine (Fig.3). This may be due to an unknown chemical modification of the substance under the influence of ultraviolet light. Therefore, all values of the induced or spontaneous histamine release were corrected for the total amount of detectable histamine so that the observed decline of total histamine with increasing UVC doses did not interfere with the data presented in Figures 1 and 2.



**Fig. 3.** Decrease of the amount of detectable total histamine after UVC-irradiation within those cell suspensions used for the histamine release experiments according to Figure 1.

There was no statistically significant correlation between the percentage of induced histamine release (40-80%) of the total histamine and the inhibitory effect of UVC (data not shown); this indicates that no “spare mechanisms” permit a histamine release that UVC does not influence.

## DISCUSSION

The results presented in this paper show that specific mechanisms of MC degranulation are highly sensitive to UVC irradiation (6). The 1,000-fold higher efficiency of UVC compared to the doses of UVB required for comparable effects might be explained by the strong absorption and functional alteration of membrane proteins (7). Furthermore, since the inhibitory effect of UVC can be detected immediately after irradiation, the involvement of nucleic acids is rather unlikely (8).

Due to the larger difference between the inhibitory and the cytotoxic action of UVC (the latter expressed as % spontaneous histamine release) on MCs compared to that of UVB, we suggest reconsideration for the use of small UVC doses for the therapy of *Urticaria pigmentosa*, psoriasis, and anaphylactic skin reactions.

A detailed analysis of the mechanisms of the UVC-induced inhibition of MC degranulation would require a complex biochemical and enzymological analysis. Therefore, we approached this problem in another manner by using two substances which induce histamine release from MCs by different mechanisms and by two different receptors.

The significantly different effects of UVC on the mediator release by 48/80 and A23187 permit the first conclusions. Generally, the induced histamine release by these compounds should be very sensitive to UVC-irradiation if it is completely regulated via enzyme systems located at the cell membrane. However, unlike UVB and UVA, UVC irradiation is almost entirely absorbed by the cell membrane (9).

The above hypothesis seems to be in accordance with the strong inhibition of histamine release by compound 48/80 since the action of this compound is independent of the intracellular cAMP metabolism. However, presumably, it depends on the membrane receptor, the calcium ionophore, and the phospholipid metabolism in the cell membrane (10).

Using the Ca<sup>2+</sup> ionophore A23187 eliminates the essential role of functioning systems for the opening of the native Ca<sup>2+</sup> ionophore and seems to reduce the importance of the phosphatidylserine metabolism during MC degranulation; this might explain the low UVC sensitivity of A23187-induced histamine release.

## CONCLUSIONS

In this study, we found that A23187 and compound 48/80 activate histamine release, an effect inhibited by UVC irradiation. Of course, these preliminary interpretations of our results are highly speculative. However, on the other hand, the results seem to justify the conclusion that the inhibition of histamine release from MCs by UVC irradiation might be a promising new therapy and approach for the analysis of MC degranulation mechanisms.

### *Conflict of interest*

The author declares that they have no conflict of interest.

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