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MMP-1 and IL-6: novel biomarkers to identify phototoxic chemicals

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INTRODUCTION & AIM

Photoallergy can be considered a special type of contact hypersensitivity, in which UV light activates the allergen and, therefore, the physiological mechanisms involved in the development of symptoms. In the case of pharmaceuticals, preclinical trials should include phototoxicity and photoallergy assays to ensure their safety. However, nowadays there is still a lack of non-animal methods to predict potential photoallergic reactions. Knowledge of the pathophysiological mechanisms of photoallergic contact dermatitis at different levels, such as molecular and cellular ones, is thus an important field of research. In this sense, this work explores the use of a cell line of skin keratinocytes to develop a vitro assay to identify phototoxic molecules and discriminate between photoirritant and photoallergic by differential secretion of humoral molecules.

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METHOD

To achieve this goal, keratinocytes have been exposed to different chemicals at various concentrations with well-known phototoxic potential concomitantly with 4 J/cm2 UVA or maintained in dark. After 24 hours post-incubation cell viability was determined and the concentration that induces an 80% of cell viability in dark and UVA conditions was calculated (Figure 1). Then, the secretion of different metalloproteinases (10) and inflammatory cytokines (40) in supernatant was evaluated by semi-quantitative arrays (RayBiotech).

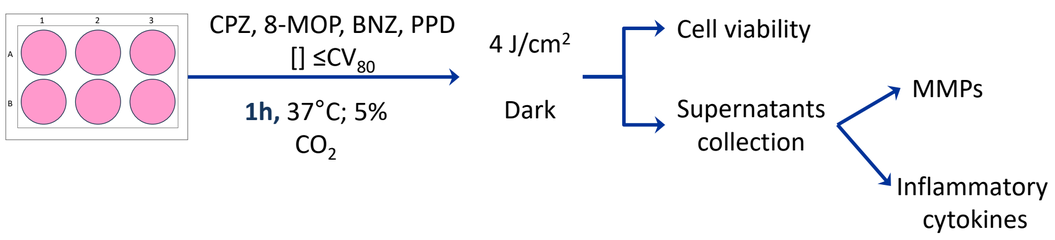
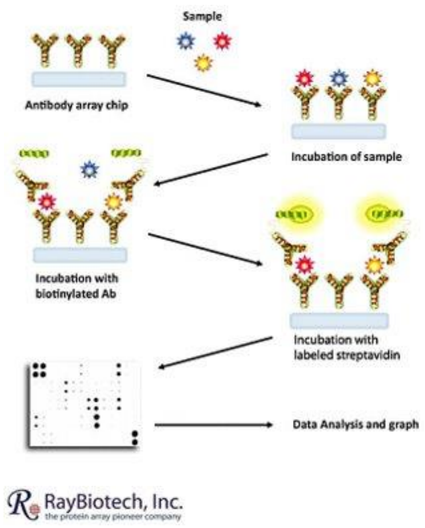


Figure 1. Schematic representation of the experimental protocol, including sample irradiation and supernatant collection steps**.** The chemicals assayed were Chlorpromazine (CPZ, photoirritant and photoallergen); 8-methoxypsoralen (8-MOP, photoirritant); Benzophenone (BNZ, photoallergen) and p-phenilendyamine (PPD, allergen)



Amersham Imager 680 UV
Amersham ImageQuant TL analysis software

Semi-quantitative

Figure 2. Steps of the semi-quantitative array and the instrument to detect chemiluminescence signal

RESULTS & DISCUSSION

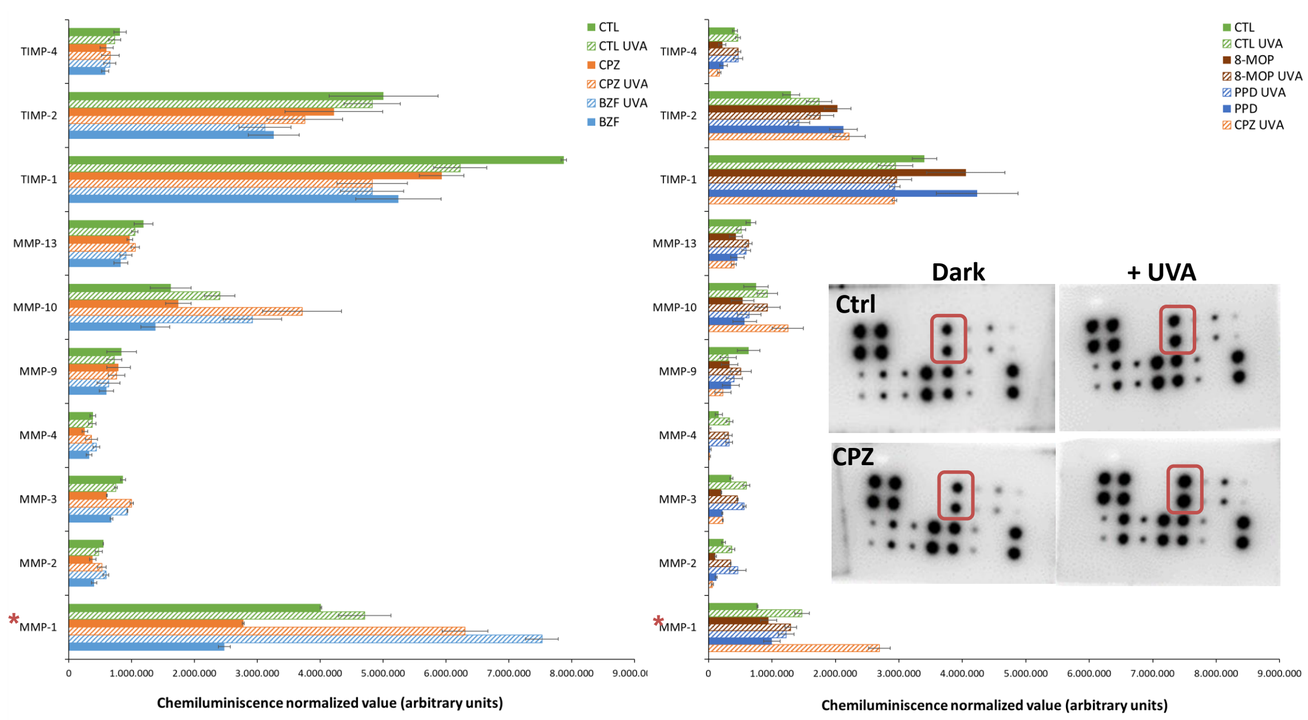


Figure 3. MMP expression regulation by different compounds under dark and UVA 4J/cm2. MMP-1 is upregulated by chlorpromazine and benzophenone under irradiated conditions.

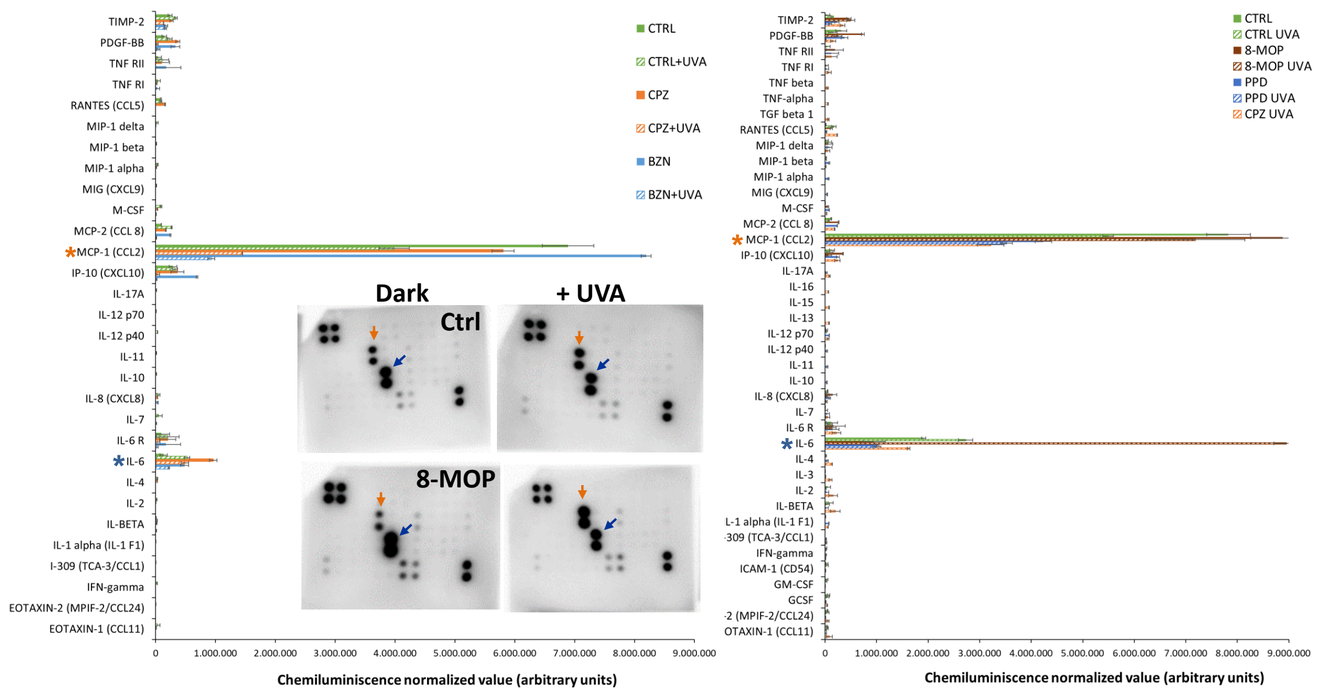


Figure 4. Inflammatory cytokines expression regulation by different compounds under dark and UVA 4J/cm2. Interleukin-6 and MCP-1 show upregulation by 8-Methoxypsolaren under irradiated conditions.

CONCLUSION

Results indicate that MMP-1 and IL-6 may serve as valuable biomarkers to discriminate between photoirritant and photoallergic reactions. Specifically, the differential expression patterns of these mediators suggest distinct underlying inflammatory pathways, making them promising candidates for improving the accuracy of in vitro phototoxicity and photoallergy testing.

FUTURE WORK / REFERENCES

Next steps include evaluation of the release of both biomarkers using a more quantitative and sensitive assay (ELISA), to confirm and strengthen the preliminary findings. The number and diversity of tested chemicals will be increased to ensure the robustness and reproducibility of the results, as well as to better assess the predictive value of MMP-1 and IL-6 in differentiating photoirritant and photoallergic responses.