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Stratum Corneum as a Sampling Matrix for Biomarker-Based Assessment of Solar Ultraviolet Exposure among Outdoor Workers

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Abstract

Introduction: Outdoor workers experience substantial solar ultraviolet radiation (UVR) exposure, yet related occupational skin diseases remain under-recognized. Early identification of biological changes induced by UVR is important for prevention. The stratum corneum (SC), the outermost epidermal layer, contains biochemical components responsive to UVR and can be sampled non-invasively, suggesting its potential as a biomarker source.
Methods: We conducted a structured literature review using major scientific databases focusing on UVR exposure, occupational health, and SC-based biomarkers. Papers describing the physiology of UVR exposure, established measurement methods, occupational risk profiles, and potential SC biomarkers, including urocanic acid (UCA) isomers and immunological mediators, were evaluated based on relevance and methodological rigor.
Results: Solar UVR, classified as a Group 1 carcinogen, induces acute and chronic skin effects. Outdoor workers receive cumulative UVR doses two to four times higher than indoor workers. Tape stripping enables minimally invasive SC collection suitable for biochemical, microscopic, and immunological analysis. Among potential markers, the trans- to cis-urocanic acid isomerization ratio demonstrates consistent UVR-dose responsiveness and correlates with exposed anatomical sites. Several cytokines involved in inflammation and UVR-induced immunomodulation may complement UCA analysis, although their consistency across studies varies.
Conclusion: The SC provides a practical matrix for assessing solar UVR exposure among outdoor workers. UCA isomer ratios represent the most promising SC biomarker, supported by mechanistic and empirical evidence. Standardization of sampling, analysis, and interpretation is required before incorporation into occupational surveillance programs.
Keywords: ultraviolet radiation, biomarkers, stratum corneum, outdoor workers, urocanic acid

Abstrak

Pendahuluan: *Pekerja luar ruangan mengalami pajanan radiasi ultraviolet matahari (UVR) yang substansial, namun penyakit kulit akibat kerja terkait tetap kurang dikenali. Identifikasi dini perubahan biologis yang disebabkan oleh UVR penting untuk pencegahan. Stratum korneum (SC), lapisan epidermis terluar, mengandung komponen biokimia yang responsif terhadap UVR dan dapat diambil sampelnya secara non-invasif, menunjukkan potensinya sebagai sumber biomarker.*
Metode: *Kami melakukan tinjauan literatur terstruktur menggunakan database ilmiah utama yang berfokus pada pajanan UVR, kesehatan kerja, dan biomarker berbasis SC. Makalah yang menggambarkan fisiologi pajanan UVR, metode pengukuran yang ditetapkan, profil risiko pekerjaan, dan potensial biomarker SC, termasuk isomer asam urocanic (UCA) dan mediator imunologis, dievaluasi berdasarkan relevansi dan ketelitian metodologis.*
Hasil: *UVR matahari, diklasifikasikan sebagai karsinogen Grup 1, menginduksi efek kulit akut dan kronis. Pekerja luar ruangan menerima dosis UVR kumulatif dua hingga empat kali lebih tinggi daripada pekerja dalam ruangan. Tape stripping memungkinkan pengumpulan SC minimal invasif yang cocok untuk analisis biokimia, mikroskopis, dan imunologis. Di antara penanda potensial, rasio isomerisasi asam trans ke cis-urocanic menunjukkan respons dosis UVR yang konsisten dan berkorelasi dengan area kulit yang terpajan. Beberapa sitokin yang terlibat dalam peradangan dan imunomodulasi yang diinduksi UVR dapat melengkapi analisis UCA, meskipun konsistensinya di seluruh penelitian bervariasi.*
Kesimpulan: *SC menyediakan matriks praktis untuk menilai pajanan UVR matahari di antara pekerja luar ruangan. Rasio isomer UCA mewakili biomarker SC yang paling menjanjikan, didukung oleh bukti mekanistik dan empiris. Standarisasi pengambilan sampel, analisis, dan interpretasi diperlukan sebelum dimasukkan ke dalam program pengawasan kedokteran kerja.*
Kata kunci: *ultraviolet radiation, biomarkers, stratum corneum, outdoor workers, urocanic acid*

Introduction

Research on occupational solar ultraviolet radiation (UVR) exposure is increasingly relevant, particularly for outdoor workers who experience high cumulative exposure throughout their working years. Solar UVR is recognized as a Group 1 carcinogen and contributes to acute sunburn, photosensitivity, and chronic conditions such as photoaging, actinic keratosis, and skin cancers [Figure 1]. Despite the severity of these outcomes, occupational UVR-related skin diseases remain underdiagnosed in many countries, including Indonesia. [1–3]

Solar UV exposure is influenced by environmental factors, such as atmospheric composition, altitude, cloud cover, and reflectance, as well as individual factors including phototype, behaviors, and protective practices. Occupational factors further amplify UVR exposure due to working hours, work posture, and reflective materials in the environment.[8]

Given the growing burden of UVR-induced disease, the identification of reliable, minimally invasive biomarkers is needed for early detection and risk assessment. The stratum corneum (SC), accessible through tape stripping, contains several UV-responsive biochemicals that may serve this purpose [Figure 2]. In this article, we review the scientific evidence supporting SC components, particularly urocanic acid (UCA), as potential biomarkers of UVR exposure among outdoor workers.[3]

Methods

We conducted a comprehensive literature review of scientific publications related to UVR exposure, occupational risk, and stratum corneum biomarkers [Figure 3]. Searches employed combinations of the keywords: *work* OR worker OR employee* OR labourer* OR laborer* OR working OR workplace OR occupation* AND ultraviolet AND biomarker AND stratum corneum*

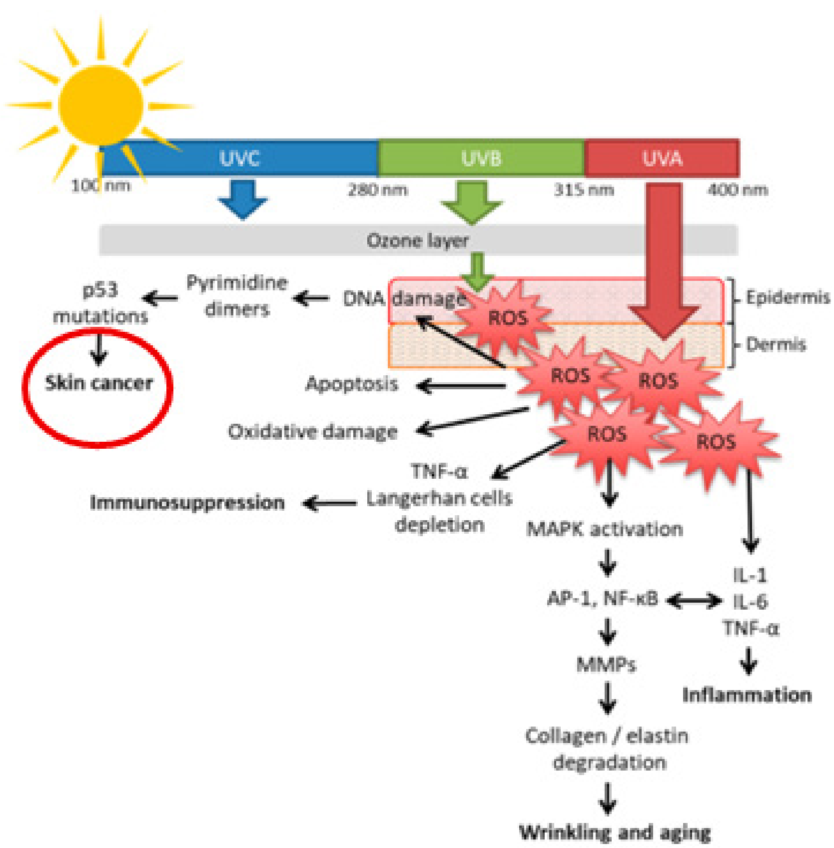

Figure 1. Solar ultraviolet radiation (UVR), UV signaling pathway and the mechanisms of its main biological effects on the skin (not all biomarker shown in this figure)[11]

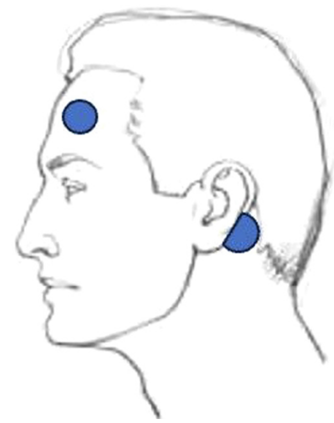

Figure 2. Sampling sites: F and E skin locations. E denotes retroauricular skin, and F denotes forehead skin

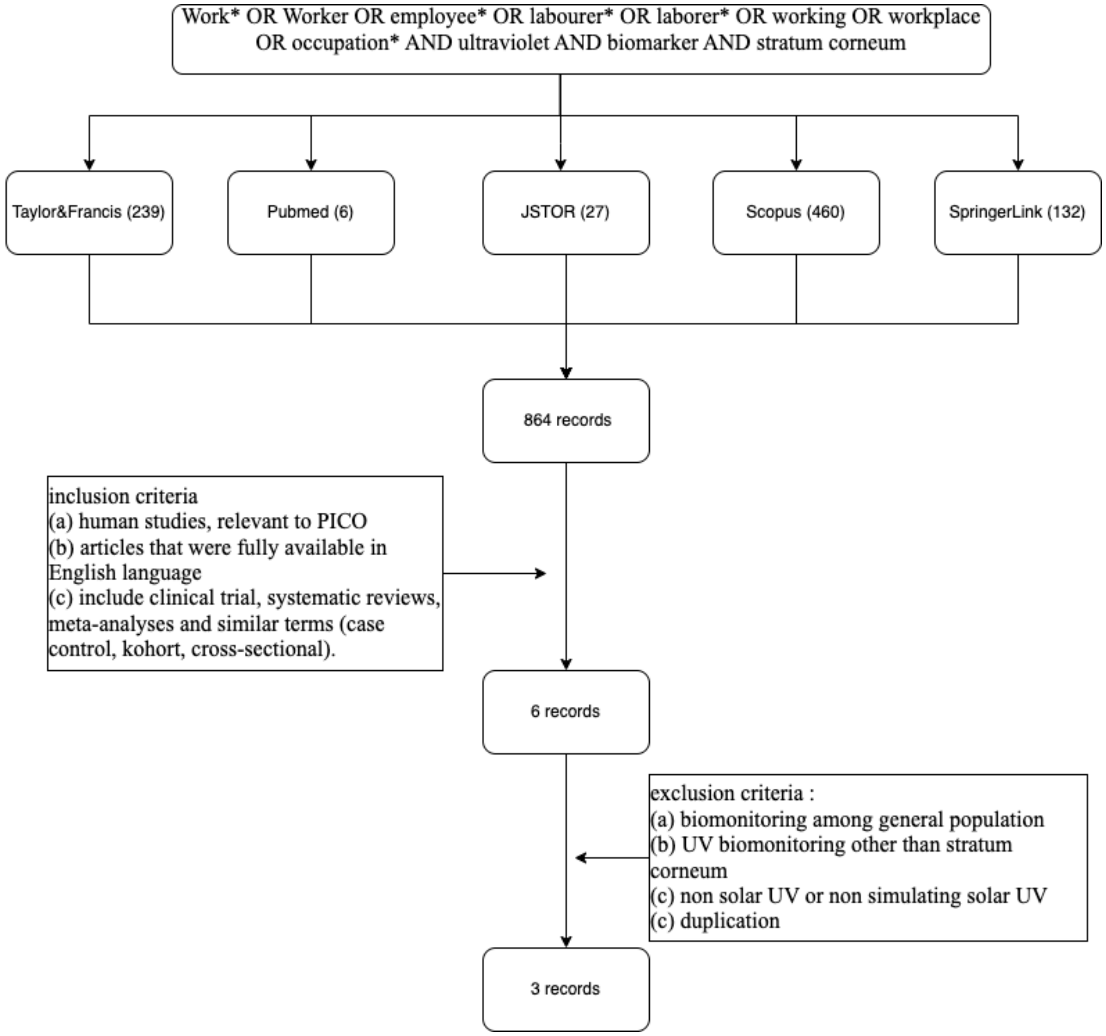

Figure 3. Literature selection process

in five major journal that are Pubmed, Scopus, JSTOR, Taylor&Francis, and SpringerLink.

Inclusion criteria were (a) human studies and relevant (b) articles that were fully available in English. (c) include clinical trial, systematic reviews, meta-analyses and similar terms (cross-sectional, case control, kohort). Exclusion criteria were (a) biomarker among general population, and (b) UV biomarker other than stratum corneum (c) non solar UV or non-simulating solar UV(d) duplication.

Critical appraisal was performed to evaluate study design, analytical methods, relevance of biomarkers, and consistency of findings.

Results

Solar UVR Exposure Among Outdoor Workers

Outdoor workers from various job type, regularly receive UVR doses exceeding occupational exposure limits designed for artificial UV sources. Daily exposures commonly range from 6 to 28 standard erythemal doses (SED) depend on various factor [Figure 4], with annual cumulative doses reaching 400–600 SED, two to three times that of indoor workers. UVB is responsible for erythema and DNA photodamage, whereas UVA penetrates the dermis and contributes to photoaging and immunomodulation.[7,8]

The Stratum Corneum as a Sampling Matrix

The SC consists of terminally differentiated corneocytes with low water content, forming the first barrier against environmental insults [Figure 2]. Tape stripping allows sequential removal of corneocytes with minimal discomfort and very low risk, facilitating large-scale sampling in occupational settings. Harvested SC can be subjected to microscopy, high-performance liquid chromatography (HPLC), immunoassays, or atomic force microscopy.[3]

Urocanic Acid as a UVR-Responsive Biomarker

UCA is synthesized from histidine as trans-UCA and accumulates physiologically in the epidermis. UVR induces photoisomerization to cis-UCA in a dose-dependent manner, with a photostationary endpoint of roughly equal proportions. UVR doses below the erythema threshold are sufficient to produce measurable increases in cis-UCA.[4,9]

Studies consistently show:[4–6]

- Higher cis-UCA proportions at chronically exposed sites compared with covered regions.
- Inter-individual variation in total UCA levels, but stable intra-individual patterns.
- Persistence of cis-UCA elevations for 1–2 weeks, suggesting utility for short-to-medium term UVR assessment.

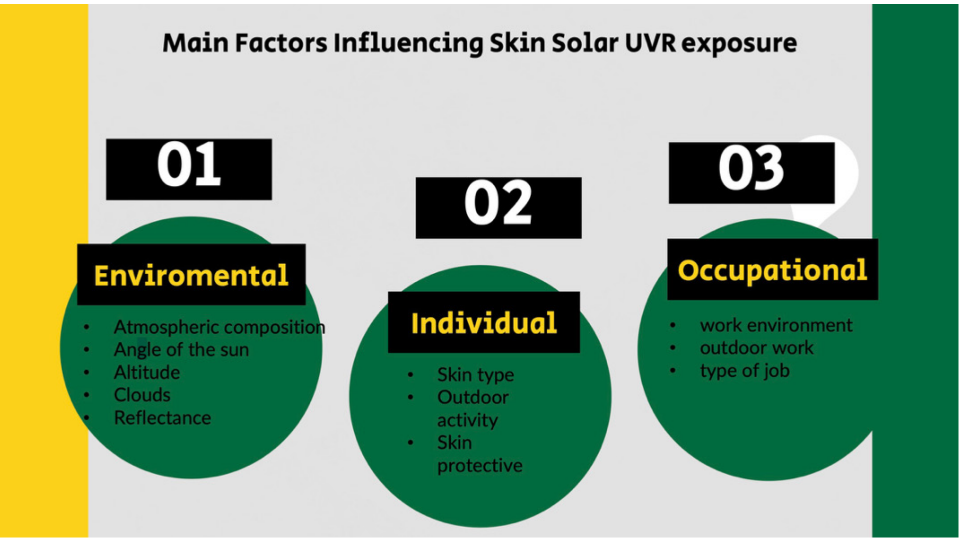

Figure 4. Main factor influencing skin solar UVR exposure[7,8]

The cis-UCA/total UCA ratio, measured by HPLC-UV, corrects for baseline differences and provides a robust indicator of UVR exposure. [4,9]

Immunological Markers in the Stratum Corneum

Collecting SC-samples was fast and easy, and several UV-biomarkers (IL-18, IL-8, CCL27, and GM-CSF) showed higher levels for sun-exposed (fore-head, face) compared to less exposed body parts (ear). There was no significant difference in various solar UV biomarker levels between OW and IW.[5]

Several cytokines, such as IL-1α, IL-1RA, CCL4 IL-18, IL-8, CCL27, and GM-CSF, participate in UVR-induced inflammatory pathways and may be measurable in the SC. However, the reproducibility and specificity of these markers vary across studies, limiting their current utility compared with UCA isomers. [4–6]

Discussion

The biomarkers discussed in this review predominantly reflect early biological effects of solar ultraviolet radiation (UVR) exposure and should not be interpreted as clinical disease markers. Tape stripping provides a minimally invasive and cost-effective approach that is readily applicable in occupational settings and compatible with high-throughput biomarker analyses.[4–6]

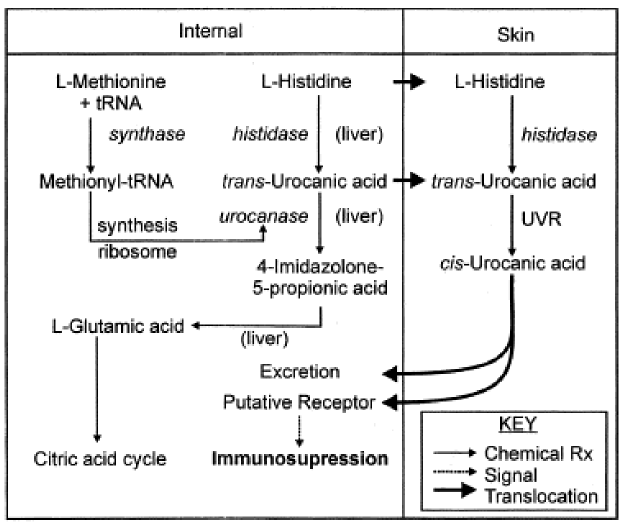

Figure 5. Biochemistry and photochemistry of urocanic acid[10]

Biomarker (pg/µg Protein)	E (Median with IQR)	F (Median with IQR)	Adjusted *P*-value[1]	IW (Median with IQR)	OW (Median with IQR)	Adjusted *P*-value	IW/OW × E/F[2]
cUCA[3]	0.504 (0.354–0.610)	0.574 (0.437–0.650)	.002	0.439 (0.354–0.553)	0.620 (0.557–0.660)	.002	0.024
Total UCA	7.733 (5.437–10.010)	4.612 (2.677–7.481)	.002	6.270 (3.658-8.608)	6.165 (3.300–9.180)	.317	0.444
IL-1RA	222.2 (113.9–374.100)	486.2 (336.700–636.600)	.002	392.200 (172.100–628.700)	322.900 (197.700–469.800)	.306	0.118
IL-1α	66.41 (47.870–128.800)	19.510 (9.474–48.130)	.002	53.110 (28.610–89.880)	41.260 (17.350–65.950)	.309	0.997
IL-1RA/IL-1α	2.516 (1.622–5.456)	19.230 (11.690–38.440)	.002	9.085 (2.162–18.030)	6.941 (2.893–26.580)	.589	0.206
IL-18	0.438 (0.181–1.393)	1.666 (0.341–5.672)	.002	0.691 (0.033–3.885)	0.670 (0.339–2.388)	.172	0.171
CCL27	0.121 (0.080–0.181)	0.136 (0.095–0.254)	.299	0.168 (0.010–0.302)	0.109 (0.074–0.171)	.306	0.421
CCL17	0.014 (0.010–0.025)	0.017 (0.012–0.023)	.551	0.015 (0.010–0.025)	0.016 (0.011–0.022)	.299	0.773
CCL4	0.203 (0.128–0.254)	0.256 (0.191–0.307)	.006	0.203 (0.136–0.281)	0.242 (0.191–0.306)	.028	0.445
MMP-9	1.056 (0.457–1.884)	0.726 (0.261–1.979)	.306	0.739 (0.260–1.375)	1.065 (0.443–2.340)	.396	1.000
VEGF-A	0.300 (0.235–0.434)	0.372 (0.280–0.466)	.111	0.372 (0.272–0.452)	0.297 (0.236–0.416)	.309	0.504
15-HETE (pg/tape)	118.700 (45.580–359.200)	354.500 (167.200–597.300)	.002	327.400 (66.760–591.600)	195.400 (48.010–402.600)	.266	0.141
CNO (protrusions/400 μm^2)	184.500 (160.100–222.900)	246.100 (206.100–282.000)	.002	200.600 (162.800–259.300)	222.300 (177.300–262.600)	.523	0.570

Abbreviations: 15-HETE, 15-hydroxyeicosatetraenoic acid; CNO, circular nano object; cUCA, cis-urocanic acid; IQR, interquartile range; IW, indoor worker; MMP-9, matrix metalloproteinase 9; OW, outdoor worker; SC, stratum corneum.

Data are given as median and interquartile ranges. E denotes retroauricular skin, and F denotes forehead skins.

[1]Differences between the 2 skin sites and between IWs and OWs were tested by the linear regression mixed model. *P*-values were adjusted for multiple testing using Benjamini–Hochberg procedure.

[2]Combined interaction effect between IWs and OWs and skin locations F and E.

[3]Relative amount of cUCA (cUCA/total UCA).

Figure 6. Stratum Corneum Biomarker Levels (cUCA and CCL4)) on the Forehead (F) and Behind the Ear (E) measured in IW (indoor workers) and OWs(outdoor workers) got significant value (p<0,05)[4]

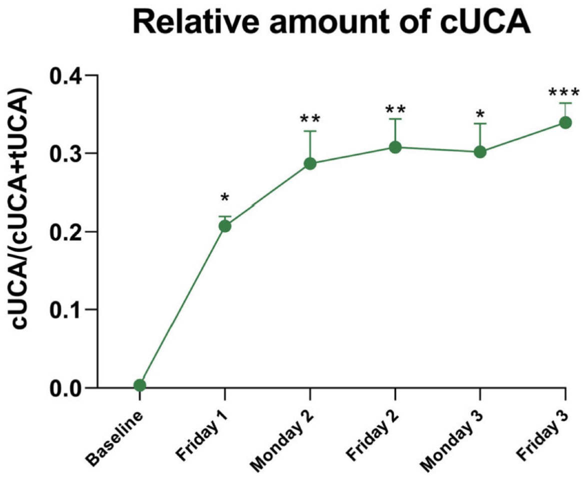

Figure 7. Relative amount of cUCA (cUCA/(cUCA + tUCA)) (n=10). Data are presented as mean and corresponding standard error of the mean. Changes from baseline at different time-points were tested by repeated-measures ANOVA *p < 0.05, **p < 0.01 and ***p < 0.001.[6]

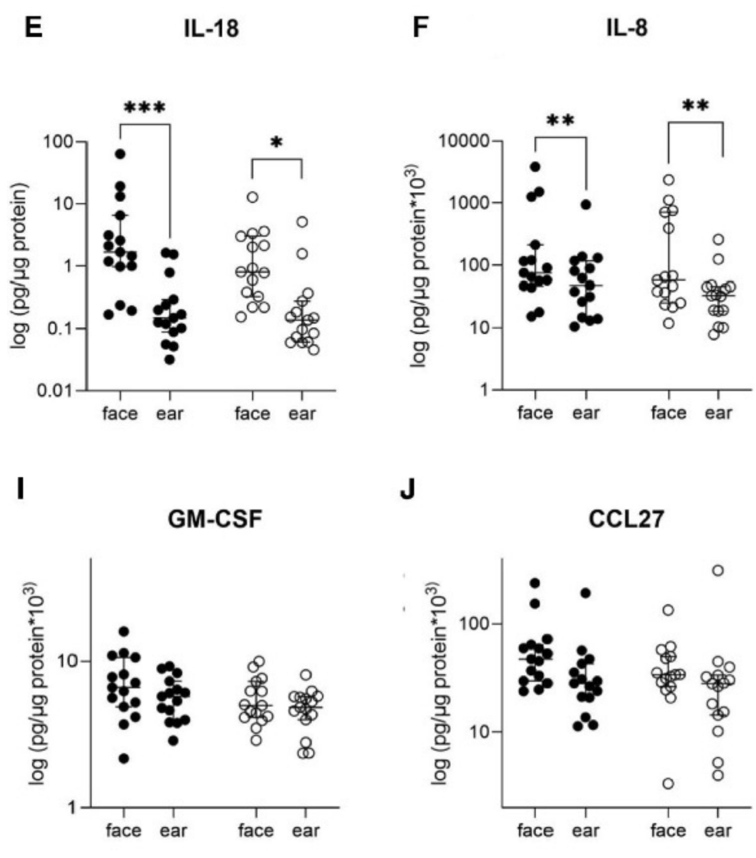

Figure 8. Overview of stratum corneum concentrations of several markers measured in outdoor and indoor workers. Legend: Black dot : outdoor worker, White dot : indoor worker. Data are presented as median with interquartile ranges. Differences in concentrations between both groups were tested using Mann-Whitney U-test. Differences in concentrations between sample locations (forehead and ear) were tested using Wilcoxon ranking tests. p <0.05.[5]

Biomarker (pg/μg protein)	Baseline M (IQR)[a]	Friday 1 M (IQR)	Monday 2 M (IQR)	Friday 2 M (IQR)	Monday 3 M (IQR)	Friday 3 M (IQR)
IL-1α	59.2 (44.6; 75.9)	51.1 (27.2; 73.0)	39.0 (28.6; 71.5)*	45.6 (26.2; 59.0)**	41.1 (26.1; 66.1)**	39.7 (22.1; 66.0)**
IL-8 ($\times 10^{-3}$)	10.9 (5.6; 16.9)	7.71 (4.0; 15.8)	6.71 (4.5; 9.8)	10.1 (3.93; 16.3)	6.8 (2.3; 11.1)	4.24 (3.0; 9.4)
IL-1RA	237 (82; 324)	261 (80; 305)	181 (96; 263)	198 (92; 253)	211 (106; 281)	206 (94; 298)
IL-1RA/IL-1α	3.52 (1.6; 5.9)	4.1 (1.8; 6.7)	3.9 (2.0; 6.8)	4.4 (2.0; 7.5)	5.3 (1.8; 7.3)*	5.5 (2.1; 8.2)*
CCL2 ($\times 10^{-3}$)	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
CCL22	2.7 (2.1; 5.4)	1.5 (0.3; 4.0)	2.7 (0.3; 3.4)	2.2 (0.6; 3.2)	2.6 (1.9; 3.3)	1.2 (0.3; 2.8)***
CCL13	0.5 (0.37;0.71)	0.66 (0.52; 0.73)	0.51 (0.36; 0.64)	0.58 (0.52; 0.61)	0.44 (0.42; 0.60)	0.54 (0.43; 0.62)
CCL4	1.1 (0.78; 1.6)	1.1 (0.55; 1.25)	0.93 (0.45; 1.3)	0.71 (0.26; 1.0)**	0.83 (0.57; 1.3)	0.7 (0.39; 0.97)**
MMP-9	29.3 (21.3; 51.2)	30.4 (15.3; 71.2)	37.3 (22.6; 47.6)	24.2 (16.1; 31.0)	22.5 (11.7; 33.6)	20.8 (10.9; 22.5)
GM-CSF ($\times 10^{-3}$)	7.2 (4.5; 10.0)	2.5 (1.5; 6.4)***	3.7 (2.5; 7.1)	2.4 (1.5; 4.7)***	5.7 (4.6; 6.75)	2.9 (1.3; 4.8)***
VEGF ($\times 10^{-3}$)	[illegible]	[illegible]*	[illegible]	[illegible]*	[illegible]**	[illegible]***
PlGF ($\times 10^{-3}$)	29.8 (17.5; 48.5)	15.9 (10.1; 28.9)	31.1 (22.9; 40.2)	39.0 (22.4; 69.7)	60.4 (34.7; 77.4)**	58.3 (38.1; 76.9)
Flt1 ($\times 10^{-3}$)	68.8 (46.7; 161.7)	61.5 (35.5; 80.6)	49.3 (40.3; 73.4)	47.2 (28.4; 72.0)*	54.1 (28.0; 72.4)*	47.9 (33.6; 63.3)*

Data are given as median with interquartile ranges. Differences in marker concentrations between baseline and other time points were determined by repeated-measures ANOVA followed by Holm Sidak's multiple testing and are marked.
[a]Median (interquartile ranges).
*$p < 0.05$.
**$p < 0.01$.
***$p < 0.001$.

Figure 9. The stratum corneum levels of various immunological mediators at baseline and after UVR exposure measured on different time points[6]

Urocanic acid (UCA) isomers, particularly the cis-UCA fraction, demonstrate strong mechanistic relevance and consistent empirical support as UVR-responsive biomarkers. Their preferential elevation at sun-exposed skin sites and sensitivity to sub-erythemal UVR doses indicate that stratum corneum-based UCA analysis can detect early UVR exposure before the onset of overt clinical changes. [4–6]

Immunological markers show potential for evaluating chronic or cumulative solar UVR exposure by providing complementary information on inflammatory and immune responses. However, variability in their expression patterns across studies necessitates further validation. The combined assessment of UCA isomers with selected immunological markers therefore warrants investigation in future research. [4–6]

Standardization remains a critical requirement. Variability in tape-stripping procedures, anatomical sampling sites, and analytical methodologies must be minimized before stratum corneum biomarkers can be reliably integrated into occupational health surveillance programs. Establishing reference ranges across different skin phototypes and environmental conditions will further improve the applicability and interpretability of these biomarkers. [4–6]

Conclusions

The stratum corneum represents a practical matrix for non-invasive biomarker assessment of solar UVR exposure in outdoor workers. The cis-UCA/total UCA ratio is the most promising biomarker currently supported by evidence, specifically for acute UVR exposure. With standardized sampling and analysis protocols, SC-based biomarkers may support early detection strategies and complement preventive occupational safety measures.[4–8]

Three articles were included for appraisal in this scientific review. Table 8 below describes the summarized important characteristics and information conveyed by the three selected articles.

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Table 1. Summary of selected articles

No	Study	Occupational Setting/ Number of workers/ Control	Substance/ symptoms studied	Biomarker of exposure	Results		Level of Evidence
					Main conclusion of exposure	Additional information	
1	Skin Barrier and Immune Response Related Biomarkers of Solar UVR Exposure Comparing Indoor and Outdoor Workers/ Florentine L. de Boer, et al/2024	This study 29 healthy male OWs and 31 healthy male IWs, and comparison between biomarker in forehead and retroauricular. In 2 construction companies. Observational Control: Indoor worker	The study measures various biomarkers related to the skin barrier and immune response in the stratum corneum. These include cytokines, growth factors, 15-HETE, cis- and trans-urocanic acid (cUCA,tUCA), and corneocyte topography indicated by circular nano objects (CNO).	Stratum corneum (cUCA, tUCA) using HPLC-UV Immunological biomarker include CCL4 15-HETE Circular Nano Object (CNO) corneocyte surface topography	**cUCA and CCL4** got significant value both in skin sites and occupational group comparison: OW got higher value solar UV exposed skin than IW, and F got higher value solar UV exposed skin than E The stratum corneum biomarkers could effectively differentiate between indoor and outdoor workers in terms of UVR exposure and its effects on skin barrier and immune response.	**Higher Biomarkers in Outdoor Workers**: Outdoor workers had higher levels of certain biomarkers in their skin, indicating more exposure to UV radiation **Skin Barrier Changes**: The skin barrier function was more compromised in outdoor workers compared to indoor workers **Increased Immune Response**: Outdoor workers showed a stronger immune response, likely due to more UV exposure	3
2	Stimulating Sunscreen Use Among Outdoor Construction Workers: A Pilot Study/Anne J. keurentjes et. Al/2022	Stratum corneum (SC) samples for the assessment of UV-biomarkers were collected from the forehead and behind the ear from 15 OW and 15 IW. Intervention: sunblock cream Control: Indoor Worker	The tape strips collect stratum corneum on forehead and behind the ears, and analyze using high-performance liquid chromatography (HPLC-UV). The limit of detection HPLC is 0.14 μmol L^{-1}, and the lower limit of quantitation is 0.45 μmol L^{-1}.	Stratum corneum (cUCA, tUCA) using HPLC-UV Immunological markers include IL-18, IL-8, CCL27, and GM-CSF	Collecting SC-samples at the workplace is feasible and several UV-biomarkers showed to be promising in assessing UVR-exposure. The low participation rate and high loss to follow-up poses a challenge for future intervention studies	Several UV-biomarkers **(IL-18, IL-8, CCL27, and GM-CSF)** showed higher levels for sun-exposed compared to less exposed body parts. There was no significant difference in various solar UV biomarker levels between OW and IW.	3

No	Study	Occupational Setting/ Number of workers/ Control	Substance/ symptoms studied	Biomarker of exposure	Results		Level of Evidence
					Main conclusion of exposure	Additional information	
3	Tape stripping the stratum corneum for biomarkers of ultraviolet radiation exposure at sub-erythemal dosages: a study in human volunteers/Anne J. Keurentjes, et al/2020	12 volunteers were exposed to UVB-dose of 0,72 SED, 3x per week, for 3 weeks Time serial Quasi Experimental Intervention: Simulating solar UVR (Approved and standard UV-therapy device) Control : No	As candidate biomarkers, cis isomers of urocanic acid (cUCA) and 25 immunological mediators were measured in the stratum corneum	Stratum corneum (cUCA) Immunological biomarkers include IL-1RA/IL-1a and a placental growth factor (PIGF)	Stratum corneum represents a promising, non-invasive alternative to skin biopsy in detecting UVR- induced changes. **cUCA** is the marker of choice for assessment of single UVR-exposure; however, it is less suitable for cumulative UVR-dose.	Immunological markers including **IL-1RA/IL-1a and PIGF** showed gradual changes, and therefore are convenient for monitoring chronic UVR-exposure. These candidate biomarkers might facilitate assessment of the efficacy of preventive measures in the workplace and general population.	3

5. Keurentjes AJ, Kezic S, Rustemeyer T, Hulshof CTJ, van der Molen HF. Stimulating sunscreen use among outdoor construction workers: A pilot study. Front Public Health 2022;10: 857553.
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