A comparative study of UVA and UVB radiation: Mechanisms of DNA damage and repair

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ABSTRACT

Ultraviolet (UV) radiation, comprising UVA and UVB rays, poses a significant threat to human health. This review aims to elucidate the differences between UVA and UVB radiation in their ability to induce DNA damage, shedding light on the underlying molecular mechanisms involved. Understanding these mechanisms is crucial for developing strategies to mitigate the harmful effects of UV radiation. The study analyzed histological changes in UVA and UVB-exposed skin and explored matrix metalloproteinases (MMPs) and reactive oxygen species (ROS) in UV-induced skin damage. It examined DNA lesions caused by UVA and UVB radiation. UVA radiation led to dermal integrity loss, collagen breakdown, and inflammatory infiltration, while UVB radiation primarily resulted in keratinocyte proliferation. UVA-induced MMP activation accelerated collagen breakdown, whereas UVB exposure moderately increased MMP activity. UVA caused more DNA and protein oxidation, while UVB primarily induced oxidative protein modification and endoplasmic reticulum (ER) stress. UVA-induced oxidative stress and DNA damage were associated with skin cancer, premature aging, and immune suppression. UVB radiation directly interacted with DNA, forming cyclobutane pyrimidine dimers (CPDs) and pyrimidine (6-4) pyrimidone photoproducts (6-4PPs), which are strongly associated with skin cancer development. UVA and UVB radiation have distinct characteristics and induce different DNA lesions. Repair mechanisms, such as nucleotide excision repair (NER) and base excision repair (BER), play crucial roles in maintaining genomic integrity. Understanding the mechanisms underlying UVA and UVB-induced DNA damage and repair is essential for developing targeted prevention and therapeutic approaches to combat the harmful effects of UV radiation.

Keywords: ultraviolet; DNA damage; photoaging; antiaging.


INTRODUCTION

Ultraviolet (UV) radiation, a pervasive environmental factor, plays an intricate role in shaping the biological landscape, with profound implications for human health. In this scientific journal, we explore the biological effects of two key components of solar UV radiation: UVA (Ultraviolet A) and UVB (Ultraviolet B). These rays, distinguished by their distinct wavelengths and energy levels, intricately interact with biological systems, particularly DNA, culminating in divergent mechanisms of DNA damage.

This research serves as an indispensable foundation for understanding the intricate molecular processes underpinning UV radiation's impact on human biology. By elucidating these mechanisms, we expand our scientific knowledge and underscore the paramount significance of this research in the context of public health.

The implications of UVA and UVB radiation reach far beyond mere academic curiosity. The consequences encompass a spectrum of health concerns, from the insidious process of premature aging to the ominous specter of skin cancer. These deleterious effects underscore the urgent need for a comprehensive understanding of the biological consequences of UV radiation. Furthermore, within this journal's context, we explore the specialized DNA repair mechanisms that operate in response to UVA and UVB-induced damage. The comprehension of these mechanisms provides insights into fundamental biological processes and points the way toward potential therapeutic interventions aimed at bolstering DNA repair capacity.

This article aims to unravel the intricacies of UVA and UVB radiation on DNA, offering a deeper understanding of the biological impacts that underpin the importance of safeguarding human health. Beyond scientific inquiry, this research carries tangible benefits for public awareness, preventative strategies, and potential therapeutic advancements, all converging toward a healthier, UV-protected future.

Ultrasound Radiation

Ultraviolet (UV) radiation from sunlight is a pervasive environmental factor that can impact biological systems, particularly DNA, in diverse ways. UVA and UVB rays present in sunlight have distinct characteristics due to their differing wavelengths and energy levels. While UVA radiation constitutes most of the UV radiation reaching the Earth's surface, UVB radiation has higher energy levels. The interaction of these rays with biological systems, particularly DNA,
Table 1. UVA and UVB Radiation: A Comparative Analysis of Skin Cell Damage and Penetration

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<td>1. Protein Carbonylation:</td>
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<td>- Activation of AP-1 and NF-κB signaling pathways</td>
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<td>- UVB radiation directly causes skin cancer and significantly promotes carcinogenic molecular processes such as p53 and c-Myc, implying a role for UVB in initiating skin cancer. UVB directly causes skin cancer, whereas UVA damages the immune system and degrades the ECM, allowing cancer cells to invade and metastasize.</td>
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<td>DNA damage photoproduct</td>
<td>UVA radiation generates 8-oxoG, an oxidative lesion formed by the oxidation of guanine bases</td>
<td>UVB radiation directly interacts with DNA molecules, causing photochemical reactions that alter DNA structure.</td>
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<td>DNA Repair Mechanism</td>
<td>The generation of ROS leads to oxidative stress, a key contributor to UVA-induced DNA damage.</td>
<td>The MMR pathway, primarily responsible for correcting errors during DNA replication, can also recognize and repair mispairs involving 8-oxoG</td>
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<td>Skin Appearance</td>
<td>Histological changes in the skin caused by UVA radiation revealed an increase in dermis thickness and breakdown, as well as a disorder of collagen fiber, indicating skin integrity loss in the dermal layer is a possibility. The histology results also confirmed the particular characteristics of UVA-treated skin, such as inflammatory infiltration. UVA-mediated DNA damage has been linked to the development of skin cancer, premature skin aging, and immune suppression.</td>
<td>UVB-induced DNA lesions hinder normal DNA replication and transcription processes, compromising cellular function and integrity. The accumulation of UVB-induced DNA damage is strongly associated with developing skin cancers, including basal cell carcinoma, squamous cell carcinoma, and melanoma.</td>
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**Abbreviations:** UVA, ultraviolet A; UVB, ultraviolet B; AP-1, Activator Protein -1; NFkB, Nuclear Factor Kappa-B; MMP, Matrix metalloproteinases; ECM, Extracellular Matrix; P53, Protein 53; CPD, cyclobutane pyrimidine dimers; 6-4 PP, pyrimidine (6-4) pyrimidone photoproducts; 8-oxoG, 8-Oxoguanine; ROS, Reactive oxygen species; MMR, mismatch repair; NER, nucleotide excision repair; DNA, Deoxyribonucleic acid.

Leads to divergent mechanisms of DNA damage induction. Understanding these mechanisms is crucial for elucidating the impacts of UV radiation on human health, including premature aging and skin cancer.1

Skin aging is a complex process influenced by both extrinsic and intrinsic factors. External environmental factors, such as sun exposure, air pollution, smoking, and poor nutrition, primarily drive extrinsic aging. Long-term exposure to UV light, especially UVA radiation, is a principal cause of extrinsic skin aging, commonly known as photoaging. In contrast, intrinsic aging factors include genetic predisposition and internal cellular processes. While extrinsic and intrinsic factors contribute to cutaneous aging, experts suggest that external causes drive the majority of aging impacts.2

**Ultraviolet Radiation DNA Damage**

Consistent exposure to UV radiation can cause DNA damage and mutations, accelerating aging and increasing the risk of carcinogenesis. Although less energetic than UVB, UVA radiation penetrates deeper into the skin and primarily induces DNA damage by generating reactive oxygen species (ROS) and oxidative stress. UVA-induced DNA damage includes oxidized bases, single-strand breaks, DNA-protein crosslinks, and lipid peroxidation, leading to skin cancer, premature skin aging, and immune suppression.3

In contrast, UVB radiation directly interacts with DNA molecules, causing photochemical reactions that alter DNA structure. The two predominant DNA lesions induced by UVB radiation are cyclobutane pyrimidine dimers (CPDs).
and pyrimidine (6-4) pyrimidone photoproducts (6-4PPs). These UVB-induced DNA lesions disrupt normal DNA replication and transcription processes, compromising cellular function and integrity. Accumulation of UVB-induced DNA damage is strongly associated with the development of skin cancers, including basal cell carcinoma, squamous cell carcinoma, and melanoma.4

Specialized DNA repair mechanisms are employed to maintain genomic integrity and prevent the accumulation of mutagenic DNA damage.1 For 8-oxoG lesions, which result from UVA-induced oxidative stress, the base excision repair (BER) pathway plays a crucial role. BER involves specific DNA glycosylases, such as OGG1, which recognize and excise 8-oxoG, followed by DNA polymerase and DNA ligase that fill the gap and seal the repaired DNA strand.1 In contrast, the nucleotide excision repair (NER) pathway primarily recognizes and removes CPDs induced by UVB radiation. Proteins like XPC, XPA, and TFIIH recognize and verify the presence of CPDs, leading to dual incisions on both sides of the lesion, removal of the damaged DNA strand, and subsequent repair.1 Understanding the repair mechanisms for UVA and UVB-induced DNA damage is crucial for preserving genomic integrity, preventing genomic instability and increasing the risk of diseases, including cancer and premature aging. Understanding the repair mechanisms for 8-oxoG and CPDs provides insights into the molecular processes involved in repairing UVA and UVB-induced DNA damage.5 Furthermore, it highlights potential targets for therapeutic interventions to enhance DNA repair capacity and reduce the detrimental effects of UVA and UVB radiation on human health.5 This review explores the molecular basis of skin aging, the biological impact of UVA and UVB radiation on the skin, and the specialized DNA repair mechanisms involved in mitigating the damage caused by these radiations. Differences in DNA Damage of UVA and UVB are in Table 1.

Wave Length and Depth Skin Penetration
Ultraviolet (UV) radiation, specifically UVA and UVB rays, plays a significant role in the biological impact of sunlight on the skin. Understanding the distinct effects of UVA and UVB radiation on DNA and skin integrity is crucial for developing effective preventive and therapeutic strategies. This review discussion aims to summarize the key findings and implications of the differential mechanisms of DNA damage induction and the resulting histological changes caused by UVA and UVB radiation.6

UVA radiation, with longer wavelengths (315-400 nm), constitutes most of the UV radiation reaching the Earth’s surface. Although UVA radiation is less energetic, it can penetrate deeper into the skin, affecting both the epidermis and dermis.6 UVB radiation can penetrate the outer layers of the skin and reach the dermis, causing harm to various important cell populations such as keratinocytes and fibroblasts. Extensive research indicates that UVB exposure leads to damage that can result in the loss or apoptosis of skin cells.7 It is widely believed that keratinocytes, the predominant cells in human skin, are particularly susceptible to UV radiation and are likely to be the initial cells affected by its harmful effects.8

In contrast, UVB radiation, with shorter wavelengths (280-315 nm), possesses higher energy levels and directly impacts DNA molecules. Upon exposure to UVB radiation, photons are absorbed by DNA, leading to the formation of DNA lesions, particularly cyclobutane pyrimidine dimers (CPDs). CPDs are formed when adjacent pyrimidine bases become covalently bonded, distorting the DNA helix. UVB radiation primarily affects the epidermal layer, where much UVB is absorbed. The histological changes observed in UVB-exposed skin include keratinocyte proliferation in the epidermis without significant changes in the dermis, indicating an accelerated proliferative lifetime in epidermal cells.7

Molecular Effect
UVA radiation, a component of solar UV radiation, elicits a multifaceted array of biological effects that have garnered significant scientific attention. Firstly, UVA radiation has activated pivotal signaling pathways, including AP-1 and NF-κB, precipitating robust inflammatory responses. This activation is paralleled by the augmentation of matrix metalloproteinase (MMP) production, an enzyme family pivotal in extracellular matrix (ECM) remodeling, ultimately leading to the degradation of collagen and elastin fibers within the dermis. Moreover, UVA radiation’s deleterious impact extends to the immune system, as it has been observed to impair immune function. Furthermore, the insidious influence of UVA radiation encompasses the degradation of the extracellular matrix (ECM), jeopardizing tissue structural integrity. Notably, UVA radiation also raises concerns regarding its potential role in cancer metastasis, as it has been associated with facilitating the invasion and metastatic spread of cancer cells. These complex and interrelated effects of UVA radiation underscore its significance in scientific investigation and its broader implications for human health and pathology.9

In contrast to UVA, UVB radiation exerts distinct effects on biological systems. UVB treatment stands out for its propensity to increase protein carbonylation, a modification indicating oxidative damage to proteins. This process underscores the distinctive biochemical impact of UVB radiation. UVB treatment notably promotes the proliferation of keratinocytes, a pivotal cell type in the epidermis. This effect underscores UVB’s role in stimulating cellular responses associated with skin physiology. UVB radiation sets intricate molecular processes in motion, including activating key signaling pathways like p53 and c-Myc. These pathways have profound implications, suggesting UVB’s involvement in initiating the complex cascade leading to skin cancer. In striking contrast to UVA, UVB radiation directly contributes to skin cancer induction. The significant promotion of carcinogenic molecular processes such as p53 and c-Myc activation underscores this direct causative relationship. This emphasizes UVB’s role as a direct instigator of skin cancer, delineating it from UVA radiation’s immune system-damaging and ECM-degrading effects.
DNA damage photoprodut and DNA Repair Mechanism

UVB radiation initiates the formation of CPDs through DNA absorption of UVB photons. This energy absorption triggers a rapid and efficient photochemical reaction, forming cyclobutane rings between adjacent pyrimidine bases. The formation of CPDs causes bending and distortion of the DNA structure, disrupting normal replication and transcription processes. CPDs significantly impact genomic stability and are strongly associated with UVB-induced mutagenesis and carcinogenesis, particularly in skin cells. If left unrepaired, CPDs can lead to errors in DNA replication, resulting in permanent mutations and chromosomal rearrangements.7

Its primary mechanism of DNA damage induction involves the generation of reactive oxygen species (ROS) and oxidative stress, forming the oxidative lesion 8-oxoG. This oxidative DNA damage can lead to various DNA lesions and disrupt the integrity of DNA molecules within cells. The histological changes observed in UVA-exposed skin include increased dermal thickness, collagen fiber breakdown, and inflammatory infiltration, indicating potential skin integrity loss in the dermal layer. The formation of 8-oxoG by UVA radiation occurs through the interaction of UVA with endogenous chromophores, generating reactive oxygen species (ROS). These ROS induce oxidative stress and cause DNA damage, including the formation of 8-oxoG. This oxidative lesion poses a significant threat to genomic stability and is associated with various diseases, including cancer and aging.11

UVA radiation generates reactive oxygen species (ROS) within cells, leading to oxidative stress. This oxidative stress can result in the oxidation of DNA bases, particularly guanine, giving rise to 8-oxoG. The formation of 8-oxoG occurs through the oxidation of the guanine base, leading to the loss of an electron and the subsequent addition of an oxygen atom at the C8 position. This oxidative lesion disrupts the normal base pairing and can lead to mutations during DNA replication if not repaired properly.12 8-oxoG in DNA can have significant implications for genomic stability. It is a highly mutagenic lesion due to its ability to mispair with adenine during DNA replication, resulting in G-to-T transversions. If left unrepaired, these mutations can accumulate and contribute to genetic instability and the development of various diseases, including cancer. Moreover, 8-oxoG can also induce DNA strand breaks and generate additional oxidative stress, creating a vicious cycle of DNA damage and cellular dysfunction.12

Given its mutagenic potential, UVA-induced 8-oxoG has been implicated in UVA-related diseases, particularly skin cancer. The accumulation of 8-oxoG lesions in the genome of skin cells can lead to oncogenic mutations and promote malignant transformation.3 Additionally, 8-oxoG has been associated with aging, as oxidative damage accumulates over time and contributes to cellular senescence and tissue deterioration. Oxidative damage to DNA, including forming 8-oxoG, arises from the interaction of DNA with ROS generated during normal cellular metabolism and exposure to environmental factors such as ionizing radiation and UV radiation. 8-oxoG is highly mutagenic due to its ability to mispair with adenine, leading to G-to-T transversions during DNA replication. To counteract the deleterious effects 8-oxoG, cells have developed sophisticated DNA repair mechanisms that efficiently recognize and remove this lesion.3

Another literature views the formation of UVA-induced DNA damage as a complex process involving direct and indirect mechanisms. While direct DNA damage caused by UVA is well-characterized, including the formation of cyclobutane pyrimidine dimers (CPDs) and pyrimidine (6-4) pyrimidone photoproducts (6-4Ps), emerging evidence suggests that UVA-induced oxidative stress plays a crucial role in DNA damage and the formation of the oxidative lesion, 8-oxoG.13 UVA radiation significantly increases MMP activity, leading to collagen breakdown and fibroblast apoptosis. This results in the destruction of collagen fibers and the development of deep furrows in UV-exposed skin. On the other hand, UVB exposure moderately increases MMP activity, suggesting that UVB wavelengths cause milder dermal damage compared to UVA. UVA radiation induces biomolecule oxidation, leading to fibroblast death and immune cell damage. It triggers inflammatory responses by activating AP-1 and NF-κB signaling pathways, promoting MMP production and collagen/elastin fiber breakdown in the dermis.13

In contrast, UVB exposure primarily increases protein carbonylation and promotes keratinocyte growth. UVB radiation is also implicated in initiating skin cancer through molecular processes involving p53 and c-Myc.9 Another opinion is that UVA and UVB radiation produce reactive oxygen species (ROS) implicated in inflammatory reactions and skin aging. UVA radiation is associated with more DNA and protein oxidation, indicating chronic skin damage. In contrast, UVB radiation primarily causes acute injury through endoplasmic reticulum (ER) stress mediated by the unfolding protein response (UPR). This suggests that UVA may contribute to long-term skin damage, while UVB is involved in immediate and transient effects.14

The BER pathway is the primary DNA repair mechanism for repairing small, non-bulky lesions such as 8-oxoG. BER involves a series of coordinated steps, beginning with the recognition and excision of the damaged base. Specific DNA glycosylases, such as OGG1 (8-oxo guanine DNA glycosylase), recognize and remove 8-oxoG from the DNA backbone, creating an abasic site. AP endonucleases then incise the DNA strand at the abasic site, initiating the repair process. Subsequent steps involve DNA polymerase and DNA ligase, filling the gap and sealing the repaired DNA strand.10

Nucleotide excision repair (NER) is the primary repair pathway responsible for recognizing and repairing CPDs, specializing in removing bulky DNA lesions. NER begins with recognizing CPDs by a complex of proteins, including XPC, XPA, and TFIIH. These proteins identify and verify the presence of DNA distortion caused by CPDs.7 Dual incisions are then made on both sides of the lesion by the endonucleases of the NER pathway, which removes the damaged DNA strand. DNA polymerase and DNA ligase fill the gap and seal the
repaired DNA strand. Cells have evolved sophisticated DNA repair mechanisms to recognize and repair CPDs, maintaining genomic integrity. The nucleotide excision repair (NER) pathway primarily identifies and removes CPDs. In NER, a complex of proteins, including XPC, XPA, and TFIH, recognizes the DNA distortion caused by CPDs. Dual incisions are made on both sides of the lesion, removing the damaged DNA strand. DNA polymerase and DNA ligase fill the gap and seal the repaired DNA strand.7

In addition to BER and NER, alternative repair pathways can contribute to removing 8-oxoG lesions. The mismatch repair (MMR) pathway, primarily responsible for correcting errors during DNA replication, can also recognize and repair mispairs involving 8-oxoG. The involvement of MMR ensures that 8-oxoG-induced mutations are corrected even after replication. Furthermore, translesion synthesis (TLS) polymerases, specialized DNA polymerases, can bypass 8-oxoG lesions during DNA replication, allowing for the replication of damaged DNA and subsequent repair.15

Skin Appearance
Histological changes in the skin caused by UVB-induced DNA lesions hinder normal DNA replication and transcription processes, compromising cellular function and integrity. The accumulation of UVB-induced DNA damage is strongly associated with developing skin cancers, including basal cell carcinoma, squamous cell carcinoma, and melanoma.8

UVA radiation revealed an increase in dermis thickness and breakdown, as well as a disorder of collagen fiber, indicating skin integrity loss in the dermal layer is a possibility. The histology results also confirmed the particular characteristics of UVA-treated skin, such as inflammatory infiltration. UVA-mediated DNA damage has been linked to the development of skin cancer, premature skin aging, and immune suppression.14

CONCLUSION
UVA and UVB radiation, both present in sunlight, have distinct effects on DNA and biological systems. Understanding the repair mechanisms for these DNA lesions is essential for maintaining genomic integrity and preventing the accumulation of mutagenic DNA damage. Further research and interventions are necessary to improve DNA repair mechanisms and protect against UVA and UVB-induced DNA damage. Enhancing our understanding of the molecular pathways involved in UVA and UVB-induced DNA damage can facilitate the development of targeted preventive measures and therapeutic interventions.

CONFLICT OF INTEREST
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All authors contributed equally in all phases of this publication.

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REFERENCES

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