

Infrared Light: Its Significance within the Solar Spectrum and its Influence on Human Physiology and Sun Exposure?

David John Mackay Smith*

Clinician, SunDoctors Skin Cancer Clinics Noosaville, Queensland, Australia

*Corresponding author: David John Mackay Smith, Clinician, SunDoctors Skin Cancer Clinics Noosaville, Queensland, Australia, Tel: +61 7 3365 1111; E-mail: davidjmsmith8@gmail.com

Received: August 08, 2026; Accepted: August 24, 2026; Published: September 06, 2026

Abstract

The infrared wavelength of the solar spectrum constitutes approximately 40% of solar radiation reaching the ground at sea level. The shortest wavelength, near infrared (NIR or IRA) 760-1400nm penetrates epidermis, dermis and subcutaneous tissue with biological effects. High intensity artificial sources of infrared light can have deleterious effects with upregulation of matrix metalloproteinase-1. However, these wavelengths when mimicking sunlight intensity (30-35mW/cm²) can have beneficial cutaneous effects, corresponding to the irradiance of sunlight. Humans have evolved with exposure to the potentially carcinogenic effects of sun exposure successfully until the last century. We need to consider the factors that have changed to where skin cancer is one of the most frequent cancers afflicting modern Caucasian man with melanoma being responsible for a relatively high death rate amongst young adults. NIR might precondition the skin with early morning sun exposure preparing the skin for midday exposure with its higher levels of the harmful shorter wavelengths of UVA and B. With the sun low to the horizon at dawn, sunlight must pass through a thicker layer of atmosphere to reach the skin. This tends to attenuate the shorter wavelengths (UVR) that have higher intensity but less penetration, and accentuate the longer wavelengths that have less intensity but greater penetration. Thus, the red highlights in the sky and clouds seen at twilight, red light being at the longer end of the visible spectrum and potentially providing twilight protective and reparative solar radiation essential to maintain a balance between harm and beneficial effects of solar exposure.

1. Infrared Radiation within the Solar Spectrum

The spectrum of solar radiation reaching the earth's surface at sea level extends from 290 nm to greater than 1,000,000 nm. Ranging from the shortest wavelength ultraviolet (UV) making up 6.8%, Visible light (VL) 38.9% and ~40% infrared (IR) wavelengths [1].

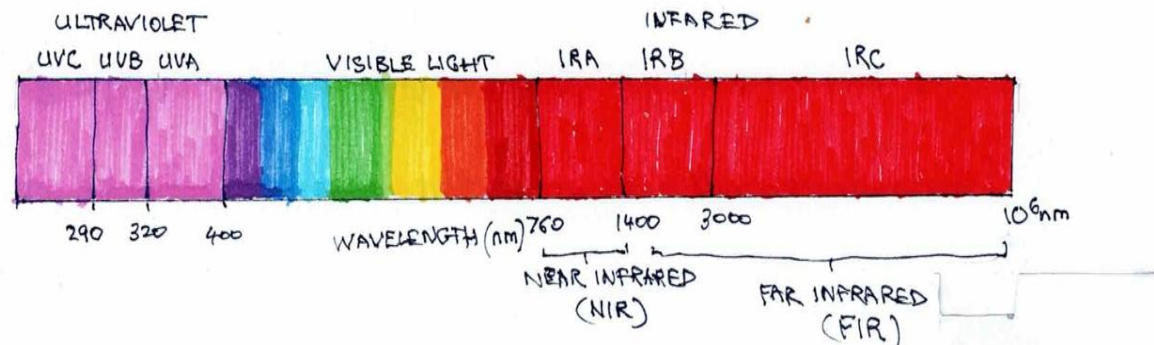


FIG. 1. The solar spectrum. UVC is blocked by the ozone layer and does not reach the earth's surface. The atmosphere also blocks the passage of selective IR wavelengths with only some of >950 nm making it to the earth's surface. Water vapour in the atmosphere absorbs the rest.

The Infrared wavelengths commence at 760 nm ranging up to 1 mm. It is divided into IR-A or near-infrared (NIR) (760 nm - 1400 nm), IR-B (1400 nm - 3000 nm) and IR-C (3000 nm to 1 mm). IR-B and C together are called far infrared (FIR). IR can penetrate epidermis, dermis and subcutaneous tissue to various extents depending on the wavelength being examined. Exposure to IR is perceived as heat [2].

The strength of electromagnetic radiation depends on the energy and number of particles or waves present and this can also be expressed as a range of wavelengths and is divided into ionising and non-ionising radiation. Non-ionising radiation has insufficient energy to completely remove electrons from atoms and molecules. Ionising radiation can create charged ions by removing electrons from atoms. UV radiation is intermediate between these two groups. Short wavelength UV can break chemical bonds causing photochemical reactions.

2. Solar Irradiance

The Sun's position relative to the Earth, the solar angle, determines irradiance levels throughout the day. As the Sun's angle changes due to the Earth's rotation, direct and diffuse sunlight are altered, peaking at solar noon when the rays hit the surface of the Earth perpendicularly. Irradiance measured in Watts per square meter (W/m^2) is determined by two angles that fluctuate through the day, the solar zenith angle (angle between the Sun and the vertical) and the solar elevation angle (the altitude of the Sun above the horizon). When the Sun is low to the horizon, irradiance is at a minimum.

This shallow angle spreads energy over a larger geographical area. Light travelling through a longer thicker path of the atmosphere with scattering and absorption of sunlight by dust and moisture before reaching the surface. The solar spectrum reaching Earth depends on many parameters, including latitude, season, meteorological conditions, ozone layer thickness and particularly on time of day.

The irradiance level of NIR is critical to trigger either beneficial effects on the skin or deleterious effects at higher levels of irradiance. Studies reporting adverse effects of NIR used artificial light sources well above the solar NIR irradiance level.

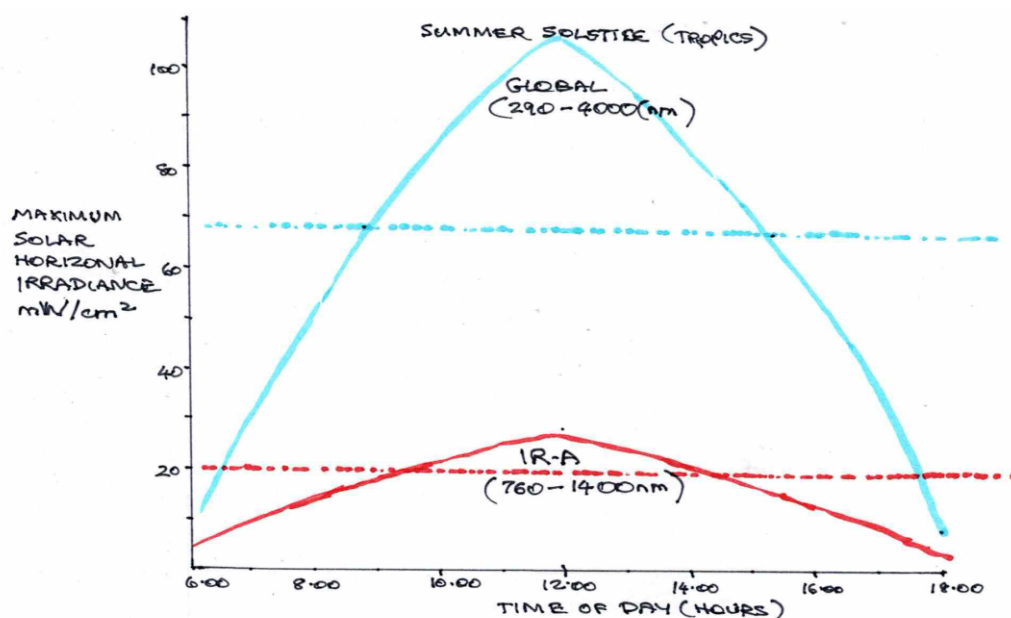


FIG. 2. Solar angle determines irradiance according to time of day, peaking at noon. The two curves represent global solar irradiance (UV-VL-IR, 290 nm - 400 nm) blue and its IR-A segment (760 nm - 1400nm) red. From 8.15 am to 3.45 pm global sun irradiance is greater than 65 mW/cm². IR-A irradiance peaks at midday at 35 mW/cm² and remains at a safe level for the length of the day (mean 20 mW/cm²). Dotted lines represent mean irradiances.

3. Beneficial Effects of Infrared Radiation

Humans have evolved in an environment bathed by solar radiation. Some wavelengths are absorbed by crucial molecules such as nucleic acids and proteins. Photochemical reactions causing damage which risks the maintenance of hereditary information and even survival of the organism. Adaptive responses, antioxidative systems and enzymatic repair mechanisms attempt to maintain an equilibrium. Considering these risks there has been a tendency to only focus on the most dangerous wavelengths of light, the UV component, but the solar spectrum is made up of a range of wavelengths with different biological effects. Much of our knowledge about solar radiation effects comes from research with monochromatic UV. The additive, synergistic or antagonistic interactions between different solar wavelengths have been largely overlooked. This particularly applies to the biological effects of infrared radiation due to the idea that these effects are mediated by heat enhancement with induction of heat shock proteins [3,4]. Sunlight, however, is polychromatic and its final effect on human skin is the result of not only the action of each wavelength individually but also the interaction between these wavelengths [5]. Research work earlier this century suggested that NIR and IR may generate protective effects as opposed to the damage induced by UVR. In 1998 Menzies et al demonstrated that noncoherent NIR radiation protected dermal fibroblasts from UVR toxicity [5]. This was followed by work suggesting that IR radiation had an effect through activation of mitochondria and induction of p53 signalling pathways [6,7].

This led to the hypothesis that pre-irradiation of skin cells with NIR could induce a natural, non-thermal cellular defence mechanism without the synthesis of proteins [8]. This research culminated in 2008 with Barolet and Boucher's paper on IR induced photoprotection where they demonstrated a reduced minimal erythema dose (MED) response following multiple LED exposures [9]. It has since been shown that IR light induces mitochondrial activation and protection.

4. Infrared Radiation Confers Resistance to UV-Induced Apoptosis

There is accumulating evidence that infrared (IR) radiation, particularly IR-A, has biological effects on human skin. It may enhance photoaging changes and carcinogenesis [10,11] but it also has been shown to have antioxidative effects through ferritin reducing free iron and thus free radicals [8]. Jantschitsch et al demonstrated that pretreatment of murine keratinocytes, *in vivo* and *in vitro*, with IR radiation reduced UV-induced apoptosis. This was through several pathways including reduction of DNA damage and upregulation of anti-apoptotic proteins. Specifically, the UV-induced downregulation of the antiapoptotic proteins FLIP_L and BCL-X_L was prevented by IR, whereas the proapoptotic protein BAX was downregulated.

This effect was not seen in DNA-repair deficient mice and suggests involvement of the nucleotide excision repair mechanism in the process [12]. This protective effect was balanced by the potential survival of UV-damaged cells having a carcinogenic effect [13].

5. Preconditioning

Preconditioning was demonstrated as early as 2005 by Decreane et al. They found that low dose UVB triggered a protective p53-dependent gene mechanism, increasing resilience of keratinocytes against future UV-B insults [14]. *In vitro* studies have shown that preconditioning of fibroblasts with NIR protecting against upcoming UVB via p53 cell signalling-induced anti-apoptotic effects [5,7]. This was followed by an *in vivo* study where test subjects were pretreated with 660 nm light as compared to controls with the degree of erythema used to assess reaction following UVB exposure. There was a sun protective effect (equivalent to SPF-15) and reduced post inflammatory hyperpigmentation observed [9].

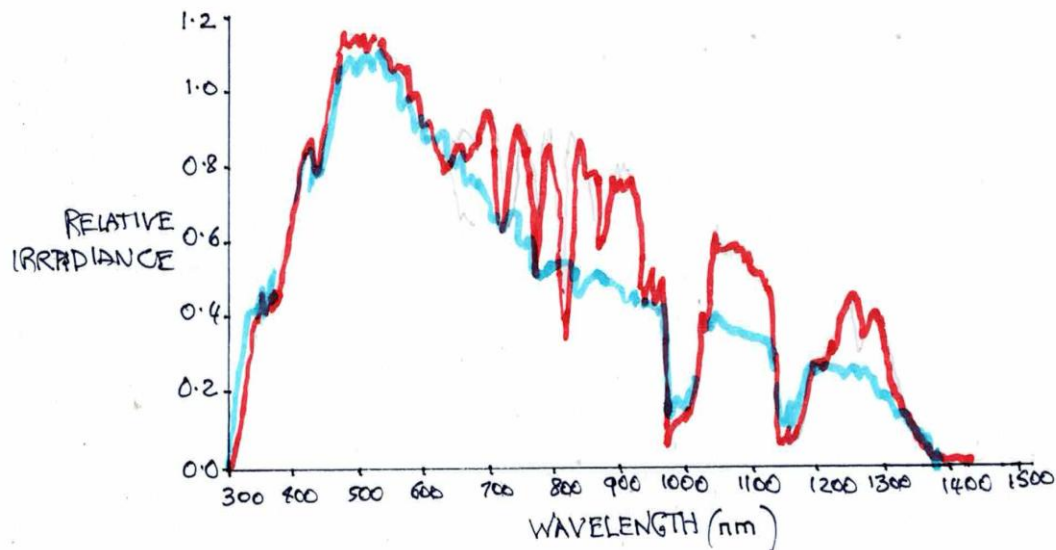


FIG. 3. Early morning (6 am) relative irradiance of sun light is higher in the VL and NIR spectrum -red line, compared to midday exposure -blue line. Calculations were made using the simple model of the atmospheric radiative transfer of sunshine (SMARTS) 2.9.5 model.

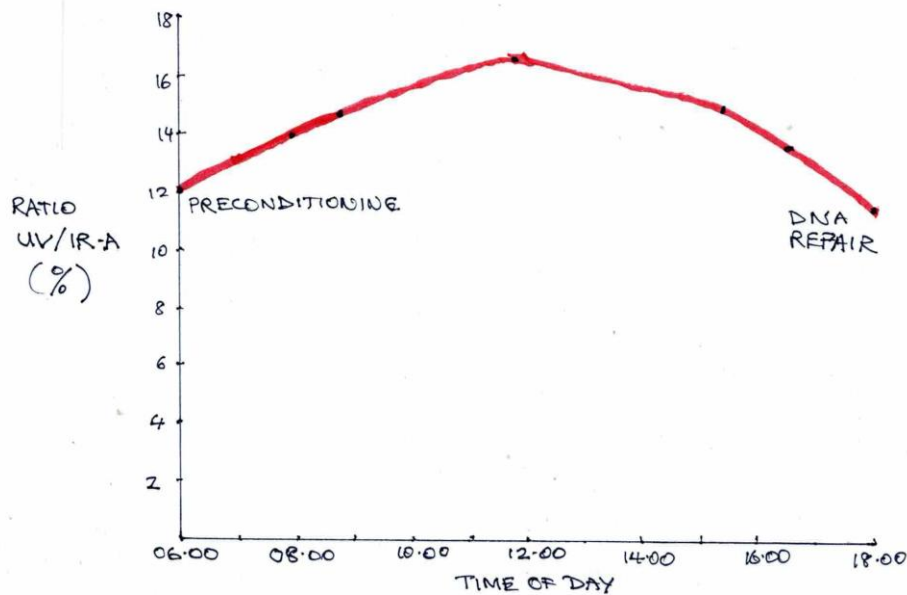


FIG. 4. Ratio of UV/IR in overhead sky throughout the day. Measured at sea level, with a cloudless in the intertropical zone (sun reaching zenith). Calculations from model of atmospheric radiative transfer of sunshine (SMARTS).

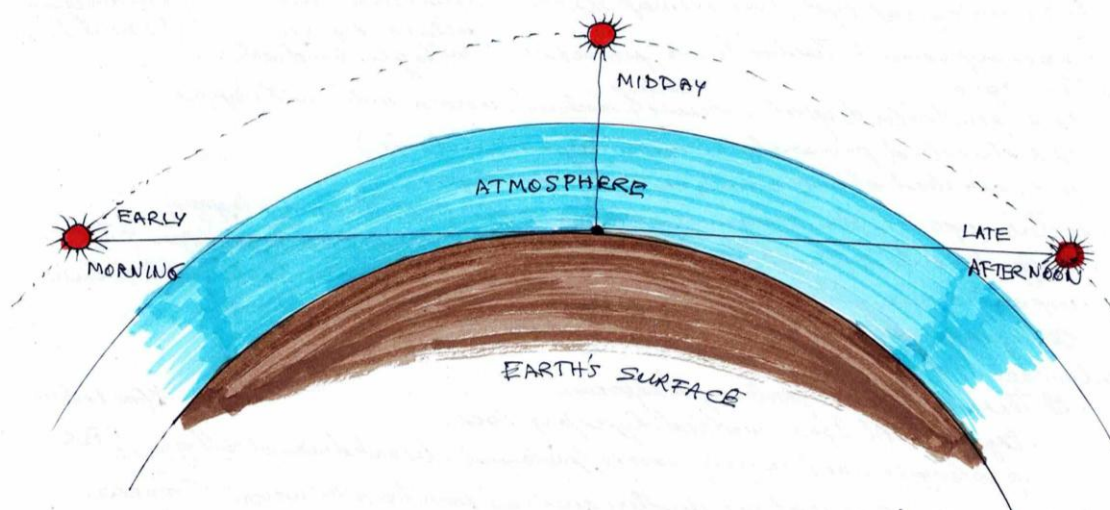


FIG. 5. Path of sunlight through the atmosphere. When the sun is low to the horizon, its rays travel through a much thicker layer of the Earth's atmosphere to reach you. Shorter wavelengths (UVR) scatter and are absorbed by ozone and air molecules in the atmosphere significantly more than longer wavelengths of VL (red) and infrared light which are less energetic but penetrate further. As seen by red highlights in the clouds and sky at dawn and dusk.

6. Evening Exposure to NIR

Evening exposure to NIR optimises mitochondrial melatonin synthesis and enhances DNA excision repair mechanisms. The natural evening environment (sunset /wood fires) Is dominated by NIR wavelengths. This is opposed to artificial light sources, particularly LED sources that lack a NIR component. This acts as a restorative signal that primes the body for night cellular defence and genetic maintenance.

Melatonin is a multifunctional antioxidant produced in the pineal gland but also produced from extrapineal sources such as the microbiota of the skin and gastrointestinal tract.

Extrapineal tissues (including skin) synthesis melatonin locally in their mitochondria via NIR exposure through activation of adenylyl cyclase acting on mitochondrial cyclic AMP (cAMP). This post translationally activates the enzymatic synthesis of melatonin within the mitochondrial matrix. Mitochondria consume oxygen to generate ATP with the release of ROS. The melatonin produced by evening light acts as an antioxidant, neutralising local ROS and preserving mitochondrial integrity overnight.

Transient low dose ROS signaling and increased mitochondrial melatonin triggers an up regulation of DNA excision repair, enhancing nucleotide and base excision efficiency. This is combined with transcription factor activation. Nuclear factor κ B (NF- κ B) and activating protein-1 (AP-1) which regulate DNA damage detection proteins. (XPA, C and D). NF- κ B translocates to the nucleus to increase aryl alkylamine N-acetyl transferase (AANAT). The final step in melatonin synthesis is generally methylation by acetylserotonin methyltransferase (ASMT) but under conditions of higher stress (exercise, solar radiation, heat exhaustion or anxiety) acetylation by AANAT can act as the final step providing a boost in synthesis to protect against higher levels of ROS.

7. The Role of Melatonin

Melatonin has a dual role in human physiology. Firstly, its involvement in the biological clock as a messenger of darkness. Secondly, its role as an antioxidant in the cellular action of NIR. Environmental light exposure suppresses its synthesis; however, it is an important antioxidant and its deficiency, through light at night, is associated with several disorders. Neurodegenerative, heart, metabolic, osteoporosis, cancer and aging. NIR, invisible but occupying a major portion of the solar spectrum, penetrates deeply promoting melatonin production. Thus, the avoidance of light at night and exposure to natural sun light during the day are equally important to human health.

Until recently all research on melatonin has focused on pineal production but there are at least four sources in vertebrates that contribute to the pool. Pineal gland, extrapineal cells, the microbiota of the skin, mouth, nose, gastrointestinal tract and dietary sources. These extrapineal sources far exceed pineal production and is used to maintain intercellular homeostasis and response to rapid changes in ROS density [15].

A phylogenically ancient molecule, believed to have emerged in primitive bacteria 2.5 billion years ago [16] and is present in all three life domains, bacteria, archaea and eukaryotes. One of the first antioxidants to have evolved and this is its primary function with other functions acquired during evolution. Acquired functions include messenger of darkness [17], regulation of reproduction in photoperiodic animals [18], sleep promotion in diurnal animals [19,20], modulation of energy production [21], anti-inflammatory [22], and oncostatic activity [23].

Pineal melatonin is estimated to be <5% of total production in mammals [24] where it is released into the blood and CSF. Most, however, is used in the cells that produce it, except the GIT that shows a post-prandial release [25,26].

It was initially accepted that melatonin was synthesised in the cytosol [27], however without convincing evidence of such. A study by Suofu et al detected AANAT and ASMT proteins in brain nonsynaptosomal mitochondria whereas the enzyme was virtually absent from the cytosol [28].

In pinealocytes, the expression of AANAT is circadian whereas this rhythm was not demonstrated in nonsynaptosomal mitochondria from neurons, indicating a functional difference between the two cell types. Continuously generated melatonin in the mitochondria of neurons provides constant protection against oxidative stress, whereas the rhythmically produced melatonin is released into the blood and CSF to convey photoperiodic alterations. The enzymes were also present in all cells tested supporting a case for diverse cellular synthesis [29-34]. Acetyl-CoA is synthesised in mitochondria, an essential substrate for AANAT, making melatonin synthesis in mitochondria more efficient than in other cellular compartments [35]. Mitochondria are a major source of ROS and reactive nitrogen species [36]. Locally synthesised melatonin providing protection. Cancer cells switch mitochondrial glucose oxidation to cytosolic glycolysis (Warburg effect) [37,38] with less acetyl-CoA production and subsequent lower melatonin levels within the mitochondria compared to normal cells [39], consistent with depressed levels of melatonin in cancer patients [40-42].

8. Mitochondria and the Retrograde Signaling Pathway

One of the defining characteristics of eukaryotic cells is the presence of mitochondria. Semi-autonomous organelles of symbiotic origin that retain a vestigial genome essential for respiratory function. The two separate but functionally interdependent genetic systems need to be coordinated, and regulatory pathways have had to evolved. Modulation of the nuclear genome expression in response to the physiological state of the mitochondria, retrograde regulation is essential [43,44]. The retrograde signalling pathway was first described in the yeast *Saccharomyces cerevisiae* a process whereby mitochondria communicate their metabolic and functional status to the cell nucleus [45].

When induced by NIR in the human this communication promotes tissue repair and cell survival by altering gene expression in favour of energy production and antioxidant defences.

This is a step wise process. Firstly, photo-acceptance and energy activation. NIR photons approximately in the range of 600-1100 nm are absorbed by Coenzyme C Oxidase (CCO), the terminal enzyme in the respiratory transport chain [46,47]. This resolves oxidative stress, improves efficiency of the transport chain and increases ATP production. This releases messenger molecules to the nucleus. ROS, in controlled low-level bursts. Nitrous oxide (NO), localised release regulates blood flow and cellular survival pathways and, Ca^{2+} which changes mitochondrial membrane potential triggering an influx of cytosolic Ca^{2+} which activates secondary messengers [48,49]. These messengers activate transcription factors that translocate from the cytosol to the nucleus shifting gene expression to promote healing.

NF-kB upregulating survival and anti-apoptotic proteins. FOXO activating cellular longevity and antioxidant protection and HIF-1 α which aids cellular adaptation to stress and promotes angiogenesis. Along with retrograde signaling pathway there is an influence on mitochondrial biogenesis. Upregulation of genes involved in wound healing, retinal protection and neuroprotection.

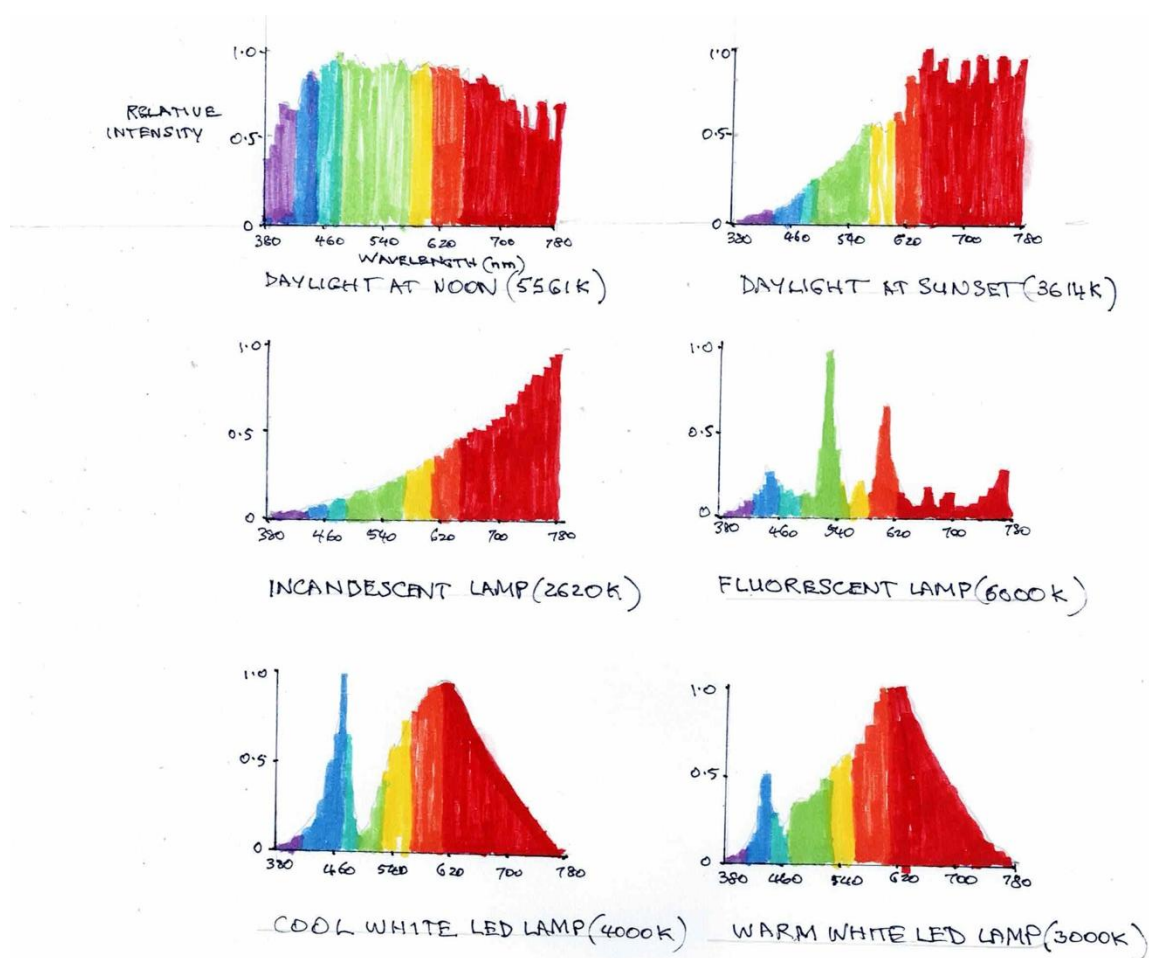


FIG. 6. Light by the source. The spectral range of modern lighting differs markedly from that of sunlight. The red and NIR wavelengths are lacking in light emitting diodes (LED) and fluorescent sources. Incandescent lighting provides a relatively high amount of light in the visible red and invisible IR spectra.

9. Conclusion

The additive, synergistic or antagonistic interactions between different solar wavelengths have been largely overlooked. This particularly applies to the biological effects of infrared radiation due to the idea that these effects are mediated by heat enhancement with induction of heat shock proteins. Sunlight, however, is polychromatic and its final effect on human skin is the result of not only the action of each wavelength individually but also the interaction between these wavelengths. The interaction between UV and Infrared wavelengths is a perfect example.

Humans are exposed to less red light than ever before. We spend more time indoors under artificial light and with efforts to conserve energy the spectrum of lighting has narrowed eliminating many red and NIR wavelengths with biological consequences (FIG. 6). The whole solar spectrum provides a range of benefits beyond Vitamin D biosynthesis by UV. The 1903 Nobel prize in Medicine recognised concentrated light as a treatment for skin tuberculosis and is now used to treat seasonal affective disorder and narrow band UV used for the management of psoriasis.

Environmental light exposure impacts the biological clock and is an important factor in the maintenance of human health. Light at night suppresses melatonin levels, a potent endogenous antioxidant, associated with a range of medical conditions. Thus, the avoidance of light at night and exposure to sunlight during the day are equally important to human well-being.

REFERENCES

1. Kochevar M, Pathak A. Photophysics, photochemistry and photobiology. In: Fitzpatrick, editor. *Dermatology in general medicine*. New York: McGraw-Hill; 1999.
2. Schieke S, Schroeder P, Krutmann J. Cutaneous effects of infrared radiation: from clinical observation to molecular response mechanisms. *Photodermatol Photoimmunol Photomed*. 2003;19(5): 228-34.
3. Lindquist S. The heat shock response. *AM Rev Biochem*. 1986;55:1151-91.
4. Maytin E, Murphy L, Merrill M. Hyperthermia induces resistance to ultraviolet light B in primary and immortalised murine keratinocytes. *Cancer Res*. 1993;53(20):4952-9.
5. Menzies S, Coulomb B, Lebreton C, et al. Non-coherent near infrared radiation protects normal human fibroblasts from solar ultraviolet toxicity. *J Invest Dermatol*. 1998;111(4):629-33.
6. Frank S, Oliver L, Lebreton-De Coster C, et al. Infrared radiation affects the mitochondrial pathway of apoptosis in human fibroblasts. *J Invest Dermatol*. 2004;123(5):823-31.
7. Frank S, Menzies S, Lebreton C, et al. Infrared radiation induces p53 signalling pathway: role in infrared prevention of ultraviolet B toxicity. *Exp Dermatol*. 2006;15(2):130-7.
8. Applegate L, Scaletta C, Panizzon R, et al. Induction of putative protective protein ferritin by infrared radiation: implications in skin repair. *Int J Mol Med*. 2000;5(3):247-51.
9. Barolet D, Boucher A. LED photoprotection: reduced MED response following multiple LED exposures. *Laser Surg Med*. 2008;40(2):106-12.
10. Kim H, Lee M, Lee S, et al. Augmentation of UV-induced skin wrinkling by infrared irradiation in hairless mice. *Mech Aging Dev*. 2005;126(11):1170-7.
11. Kim M, Kim Y, Cho K, et al. Regulation of type 1 procollagen and MMP-1 expression after single or repeated exposure to infrared radiation in human skin. *Mech Aging Dev*. 2006;127(12):875-82.
12. Jantschitsch C, Mada A, Majewski S, et al. Infrared radiation confers resistance to UV-induced apoptosis via reduction of DNA damage and upregulation of antiapoptotic proteins. *J Invest Dermatol*. 2009;129(5):1271-9.
13. Kochevar I, Taylor C, Krutmann J. Fundamentals of cutaneous photobiology and photoimmunology. In: Wolf K, Goldsmith L, Katz S, Gilchrest B, Paller A, Lefill D, editors. *Fitzpatrick's Dermatology in General Medicine*. New York: McGraw-Hill, USA; 2012.
14. Decraene D, Smaers K, Maes D, et al. A low UVB dose, with the potential to trigger a protective p53-dependent gene program, increases the resilience of keratinocytes against future UVB insults. *J Invest Dermatol*. 2005;125(5):1026-31.
15. Tan DX, Reiter RJ, Zimmerman S, et al. Melatonin: Both a Messenger of Darkness and a Participant in the Cellular Actions of Non-Visible Solar Radiation of Near Infrared Light. *Biology (Basel)*. 2023;12(1):89.
16. Tan DX, Zheng X, Kong J, et al. Fundamental issues related to the origin of melatonin and melatonin isomers during evolution: relation to their biological functions. *Int J Mol Sci*. 2014;15(9):15858-90.
17. Reiter RJ. Melatonin: the chemical expression of darkness. *Mol Cell Endocrinol*. 1991;79(1-3):C153-8.

18. Reiter RJ, Tan DX, Manchester LC, et al. Melatonin and reproduction revisited. *Biol Reprod*. 2009;81(3):445-56.
19. Shenshen Y, Minshu W, Qing Y, et al. The effect of cataract surgery on salivary melatonin and sleep quality in aging people. *Chronobiol Int*. 2016;33(8):1064-72.
20. Mousavi SA, Heydari K, Mehravaran H, et al. Melatonin effects on sleep quality and outcomes of COVID-19 patients: An open-label, randomized, controlled trial. *J Med Virol*. 2022;94(1):263-71.
21. Capolla-Neto J, Amaral F, Afeche S, et al. Melatonin, energy metabolism, and obesity: a review. *J Pineal Res*. 2014;56(4):371-81.
22. Hardeland R, Cardinali DP, Brown GM, et al. Melatonin and brain inflammaging. *Prog Neurobiol*. 2015;127-128:46-63.
23. Mota A, Jadin-Perassi B, De Castro T, et al. Melatonin modulates tumour hypoxia and metabolism by inhibiting HIF-1 α and energy metabolism pathways in the in vitro and in vivo models of breast cancer. *Melatonin Res*. 2019;2:83-98.
24. Zhao D, Yu Y, Shen Y, et al. Melatonin Synthesis and Function: Evolutionary History in Animals and Plants. *Front Endocrinol (Lausanne)*. 2019;10:249.
25. Hajak G, Huether G, Blanke J, et al. The influence of intravenous L-tryptophan on plasma melatonin and sleep in men. *Pharmacopsychiatry*. 1991;24(1):17-20.
26. Hardeland R, Pandi-Perumal SR. Melatonin, a potent agent in antioxidative defense: actions as a natural food constituent, gastrointestinal factor, drug and prodrug. *Nutr Metab (Lond)*. 2005;2:22.
27. Kappers J. Localisation of indoleamine and protein synthesis in the mammalian pineal gland. *J Neural Transm* 1978;Suppl 12:13-24.
28. Suofu Y, Li W, Jean-Alphonse FG, et al. Dual role of mitochondria in producing melatonin and driving GPCR signaling to block cytochrome c release. *Proc Natl Acad Sci U S A*. 2017;114(38):E7997-E8006.
29. Uz T, Qu T, Sugaya K, et al. Neuronal expression of arylalkylamine N-acetyltransferase (AANAT) mRNA in the rat brain. *Neurosci Res*. 2002;42(4):309-16.
30. Vishwas DK, Haldar C. MT1 receptor expression and AA-NAT activity in lymphatic tissue following melatonin administration in male golden hamster. *Int Immunopharmacol*. 2014;22(1):258-65.
31. Slominski A, Pisarchik A, Semak I, et al. Serotonergic and melatonergic systems are fully expressed in human skin. *FASEB J*. 2002;16(8):896-8.
32. Yasmin F, Sutradhar S, Das P, et al. Gut melatonin: A potent candidate in the diversified journey of melatonin research. *Gen Comp Endocrinol*. 2021;303:113693.
33. Gonzalez-Arto M, Hamilton TR, Gallego M, et al. Evidence of melatonin synthesis in the ram reproductive tract. *Andrology*. 2016;4(1):163-71.
34. Olszańska B, Majewski P, Lewczuk B, et al. Melatonin and its synthesizing enzymes (arylalkylamine N-acetyltransferase-like and hydroxyindole-O-methyltransferase) in avian eggs and early embryos. *J Pineal Res*. 2007;42(3):310-8.
35. Tan DX, Hardeland R. The Reserve/Maximum Capacity of Melatonin's Synthetic Function for the Potential Dimorphism of Melatonin Production and Its Biological Significance in Mammals. *Molecules*. 2021;26(23):7302.
36. Ott M, Gogvadze V, Orrenius S, et al. Mitochondria, oxidative stress and cell death. *Apoptosis*. 2007;12(5):913-22.

37. Reiter RJ, Sharma R, Rodriguez C, et al. Part-time cancers and role of melatonin in determining their metabolic phenotype. *Life Sci.* 2021;278:119597.
38. Fukushima A, Kim HD, Chang YC, et al. Revisited Metabolic Control and Reprogramming Cancers by Means of the Warburg Effect in Tumor Cells. *Int J Mol Sci.* 2022;23(17):10037.
39. Gaiotte L, Carvalho Cesario R, Silveira H, et al. Combination of melatonin with paclitaxel reduces the TLR4-mediated inflammatory pathway, PD-1 levels, and survival of ovarian cancer cells. *Melatonin Res.* 2022;5(1):34-51.
40. Lecarpentier Y, Claes V, Vallée A, et al. Thermodynamics in cancers: opposing interactions between PPAR gamma and the canonical WNT/beta-catenin pathway. *Clin Transl Med.* 2017;6(1):14.
41. Maestroni GJ, Conti A. Melatonin in human breast cancer tissue: association with nuclear grade and estrogen receptor status. *Lab Invest.* 1996;75(4):557-61.
42. Azama T, Yano M, Oishi K, et al. Altered expression profiles of clock genes hPer1 and hPer2 in peripheral blood mononuclear cells of cancer patients undergoing surgery. *Life Sci.* 2007;80(12):1100-8.
43. Butow R, Avadhani N. Mitochondrial signaling: the retrograde response. *Mol Cell.* 2004;14(1):1-15.
44. Ryan MT, Hoogenraad NJ. Mitochondrial-nuclear communications. *Annu Rev Biochem.* 2007;76:701-22.
45. Liu Z, Butow RA. Mitochondrial retrograde signaling. *Annu Rev Genet.* 2006;40:159-85.
46. Karu T. Primary and secondary mechanisms of action of visible to near-IR radiation on cells. *J Photochem Photobiol B.* 1999;49(1):1-17.
47. Karu TI, Pyatibrat LV, Kolyakov SF, et al. Absorption measurements of a cell monolayer relevant to phototherapy: reduction of cytochrome c oxidase under near IR radiation. *J Photochem Photobiol B.* 2005;81(2):98-106.
48. Camello-Almaraz C, Gomez-Pinilla PJ, Pozo MJ, et al. Mitochondrial reactive oxygen species and Ca²⁺ signaling. *Am J Physiol Cell Physiol.* 2006;291(5):C1082-8.
49. Cooper CE. Nitric oxide and cytochrome oxidase: substrate, inhibitor or effector? *Trends Biochem Sci.* 2002;27(1):33-9.