



Impact of Blue Light on Circadian Cycle Functions and Its Possible Alterations

María Fernanda Latorre Barragán¹, Rashell Danae Fiallos Baldeón², Frank Joel Lemache Mancheno³, Wilmer Bladimir Núñez Valencia⁴

^{1,2,3,4}Universidad Regional Autónoma de Los Andes Ambato. Ecuador.

Email: ua.marialatorre@uniandes.edu.ec¹, rashelldfb26@uniandes.edu.ec²,

frankjlm09@uniandes.edu.ec³, wilmerbnv75@uniandes.edu.ec⁴

ORCID ID: 0000-0002-9280-705X¹, 0009-0006-7562-6157², 0009-0006-7404-9538³, 0009-0001-9829-243X⁴

*Corresponding author's E-mail: ua.marialatorre@uniandes.edu.ec

Article History	Abstract
Received: 06 June 2023 Revised: 05 Sept 2023 Accepted: 11 Sept 2023	<i>The regulation of the circadian cycle, an essential process for the functioning of living organisms, including humans, is highly dependent on exposure to external light, directly influencing the sleep cycle. However, increasing exposure to artificial light from digital devices such as televisions, cell phones and computers, especially during nighttime hours, has raised concerns about its impact on the circadian cycle. This prolonged exposure alters external stimuli and, in turn, affects the production of internal chemical messengers, which can lead to metabolic, hormonal, immunological, mental and physical disorders in individuals. These findings underscore the importance of understanding the negative effects of blue light and developing strategies to counteract its impacts on human health and well-being.</i>
CC License CC-BY-NC-SA 4.0	Keywords: <i>Living organisms, Circadian regulation, Digital devices</i>

1. Introduction

All living organisms are in constant contact with the environment that surrounds them in order to adapt to it. Higher organisms, such as animals, are able to detect the cycles of light and darkness. These natural cycles stimulate physiological and behavioural changes that happen cyclically with changes in the amount of light in the environment (1). In mammals, the circadian system is considered a biological clock, due to its ability to oscillate in 24-hour cycles (1).

In humans, the circadian system is made up of an extensive network of structures located in the brain and periphery (2). This system is controlled by a small number of hypothalamic cells called the suprachiasmatic nucleus (SCN), which is located above the optic chiasm and adjacent to the third ventricle (3).

The projections of the SCN occur in the hypothalamus, thalamus and forebrain, where each one fulfils specific functions such as psychomotor performance, memory, thermoregulation, regulation of the sleep-wake cycle, etc. (3). It is in this sense, the circadian system is rigorously related to the sleep cycle, so that light is one of the most important factors when it comes to regulating sleep, since it is a primordial stimulus capable of readjusting the body's biological clock through the SCN, and which in turn is controlled by the hormone called melatonin (3). In fact, the moment the lack of light occurs, melatonin begins to be released on a regular basis to produce sleep.

The function of the circadian system is to regulate physiological processes and behaviours through the efficient adaptation of the external environment; and bodily functions such as thermoregulation, regulation of sleep cycles and secretion of hormones based on the changes of the 24-hour solar day

(4). Its proper functioning ensures that human beings can properly carry out their daily activities and in their physical, mental and emotional health (5).

In nature, the cycles of light and darkness are governed by the sunrise in the day and its fall at night, but humans have modified this natural cycle thanks to the use of artificial light inside closed environments (4). An example of this is the use of high-intensity electric bulbs, which directly affect the functioning of the circadian system, since it impacts the generation of melatonin by up to 50% (4). Another example in the current context is digital devices, since their use is part of people's daily lives, from waking up in the morning until they go to rest at night. If these electronic devices have facilitated and streamlined many of human activities, excessive use of it has caused certain alterations in the normal sleep cycle (6). This is because digital devices are emitters of an artificial blue light, which, in excess, are responsible for disturbing the ability with which the circadian system adapts to the light-dark periods of the environment (7)(8).

Therefore, it is important to note that the use of digital devices without adequate control can affect the body's circadian rhythm. As a result of its insufficiency, it produces different types of conditions, including sleep disorders that in turn are the cause of obesity, depression, anxiety, etc. (8)(9).

This literature review aims to investigate the human circadian system, the factors that influence it and the damage that occurs in contact with artificial light.

2. Materials And Methods

To carry out this bibliographic review in a rigorous and precise manner, a structured methodological approach was implemented that guaranteed the obtaining of relevant and updated information. An exhaustive search was carried out in several recognized databases in the scientific field, such as Medline, Pubmed, Scencedirect and Google Scholar, with the purpose of covering a wide range of reliable academic sources.

In order to optimize the search results, key terms relevant to the topic of study were used, such as "circadian system", "circadian rhythm", "melatonin", "blue light", "circadian disorders" and "biological clock". These terms were applied in both English and Spanish, to ensure the inclusion of scientific articles published in both languages and thus avoid language bias.

In addition to searching the databases, we carried out a thorough analysis of the reference lists of selected studies, as well as of the relevant reviews found. This strategy, known as cross-reference searching, made it possible to identify and retrieve additional articles of interest that might have been omitted from the initial search. In this way, it was possible to obtain a complete and exhaustive compilation of the available scientific literature on the subject of study.

It should be noted that clear and defined inclusion and exclusion criteria were established, with the aim of selecting the most relevant and high-quality studies. We prioritized the inclusion of original research, systematic reviews, meta-analyses and controlled clinical studies that specifically addressed the circadian system and its different aspects. On the other hand, studies that did not meet the established relevance or quality criteria were excluded.

The selection process of the studies was carried out independently by two expert researchers in the field, who objectively and systematically evaluated each article according to the predefined criteria. In case of discrepancies, a discussion and consensus were held to reach a final decision.

In summary, this literature review was carried out using a structured and comprehensive methodological approach. The combination of searching recognized databases, cross-referencing and applying rigorous inclusion and exclusion criteria resulted in a selection of relevant and high-quality scientific studies. This approach guarantees the validity and reliability of the results obtained and provides a solid basis for the development of conclusions based on scientific evidence.

3. Results and Discussion

The word circadian comes from two Greek words Circa and diem which together means around the day (10). More specifically, the circadian system can be defined as a biological process, which is responsible for generating the rhythms that regulate the stages of sleep (11,42,43).

This system can be classified into:

Circadian rhythms: 24-hour cycle in which they include physiological and behavioral rhythms such as sleep.

Diurnal rhythms: it is one that is synchronized with day and night.

Ultradian rhythms: It is a shorter rhythm and more frequently than circadian rhythms.

Infradian rhythms: are those rhythms that usually last longer than 24 hours, being the case, for example: menstruation (11).

Circadian rhythms:

The circadian rhythm plays a very important role in the physical, mental and behavioral area that respond to periods of light and dark (11,12,44,45).

Among the functions it performs are:

- Sleep schedule
- Appetite
- Body temperature
- Hormone levels
- Vigilance
- Daily performance
- Blood pressure
- Reaction time

The functioning of the circadian rhythm depends on body structures such as the hypothalamus, specifically in the SCN (2). The SCN is responsible for conducting information to the different brain and body areas through neural and humoral signals (13). One of these signals is melatonin, whose release is carried out in the pineal gland and is responsible for the regulation of circadian rhythms within the body (14). The regulation of this watch biological is given strictly and endogenously, however, it can be altered by external signals such as sunlight and temperature (11).

Factors involved in the circadian cycle

The existence of days lasting 24 hours led to the development and adaptation of living organisms to the presence and absence of light (15).

Light is defined as electromagnetic radiation with wavelengths between 380 and 750 nm which is the range visible to the human eye (16). Light radiation is manifested by the alteration in the movement of electrically charged particles. This radiation extends from Y-rays, X-rays to radio waves and long radio waves (11). Light generates illumination and can come from both natural sources such as the sun and artificial sources such as electric bulbs (16). In fact, throughout history, light and lighting have "changed", going from what is natural light to the light produced by gas lamps in the sixteenth century to lights emitted by diode (LED) used today (16)(17).

Light is an important factor for human life especially for vision since it is responsible for direct stimulation for the increase of brain activation and alertness. For this reason, changes in it can alter different non-visual responses such as endocrine, physiological and behavioural (17,46,47).

Mechanism of regulation by light

Light is one of the most reliable physical messengers for living things, as it is able to adjust the circadian rhythm and the cellular response that triggers it (18). In humans and other living beings, light is received through the retina into a group of cells called ganglion cells, which fuse in the opposite way to rods and cones. In addition, they contain a photoreceptor coupled to G proteins called melanopsin, which receives light and allows the light stimulus to regulate the lighting of the environment (19). This means that light is received and transmitted but not as non-visual information but as photosensitive information (20,48,48).

They have identified 5 types of photoreceptor ganglion cells called M1-M5. Of these, the first two are those that connect to the SCN, especially, the first that contain more melanopsin and its light response

is more accentuated. Subsequently, the transmission of information to the SCN is carried out by fibers that are projected directly from the retina. The set of these is called retinohypothalamic pathway (RHT) and are glutaminergic connections (19). The SCN is considered the master biological "clock" and generates a powerful cellular response that affects hormone secretion and physiological functions of great importance (21).

First, SCN activation causes its neurons to carry information to the paraventricular nucleus. It is then conducted to preganglionic sympathetic neurons in the intermediolateral zone in the posterior cervical ganglia, reaches their postganglionic axons and projects to the pineal gland. Here, the synthesis of melatonin, a sleep-inducing neurohormone, is produced, which is secreted into the bloodstream where the circadian cycle is regulated (19,50).

There is another method in which a structure called intergeniculated lamina (LIG) intervenes. This response occurs because the RHT separates at the height of the optic chiasm and directs the axons of its neurons to the SCN on the one hand and the LIG on the other. That is why through this system there is a potentiation of the signal received by the retina. These systems are a key element in the development of the circadian cycle and therefore are classified as synchronizers (19).

Effect of light on the circadian cycle

The effects of light on the circadian cycle can be influenced by a number of factors, including:

Spectral composition: not all light waves affect the circadian cycle, only those between 460 and 480.

The intensity: the higher the intensity of the light, the greater the effect on the circadian system.

The time of exposure to light: in this aspect exposure during night hours is more harmful.

Duration of exposure: Exposure to different durations of bright light restores the circadian pacemaker in a dose-dependent manner.

Similarly, light can induce damage to the body through three mechanisms: photomechanical, photothermal and photochemical, the latter being the most common and occurs when the eyes are exposed to a high intensity (14).

Blue light

Currently, lighting sources are used in devices such as tablets, cell phones, laptops, televisions, among others. These light sources radiate light of visible wavelengths such as blue light that has an emission spectrum between 300 to 500nm (14). This spectrum of light includes violet, indigo, blue, and inactively blue-green light. Blue-violet light has a high amount of energy, which causes irreparable damage to the cells involved in vision. However, electronic devices are not the only source of blue light, there are also natural ones such as sunlight (11).

Blue light is an external agent that can affect the whole organism and since it is a type of radiation it can affect the eyes, skin and physiological processes that occur in the body (22). In the case of the eyes, they have a wide variety of cells among which are: rods, cones and the cell of the retinal pigment epithelium that have a high amount of photo pigments so they are more sensitive to damage caused by blue light (23). One of the biochemical mechanisms of how eye damage occurs due to the effect of blue light has pointed to lipofuscin, a substance composed of lipids and proteins, as a feasible mediator of the risk of retinal damage (24). This molecule originates reactive oxygen species (ROS) when they absorb blue light generating free radicals, causing oxidative damage in the retina (24). Another problem is the visual fatigue caused by high exposure to blue light, which, being shortwave, is scattered to the cornea and lens causing a lack of focus decreasing the contrast generating a blurred or double vision (25).

The skin is an organ that is directly affected by radiation since it is the cause of photo-aging, in fact, it generates about 80% of the visible signs of aging. The way it affects is similar to that of the eyes since it generates ROS that induce photoaging, oxidative damage to DNA and hyperpigmentation. Similarly, other conditions that is produced by blue light is the alteration of circadian cycles that comprise the stages of sleep and wakefulness (22).

Dream

Sleep is a natural and physiological phenomenon very important for the integral health of humans and many animal species. This is strictly related to the circadian cycle, since during sleep consciousness, response to stimuli and metabolic rate are reduced (26). Similarly, sleep has a great importance in the immune system since it is responsible for the regulation of innate and adaptive responses, in case it is altered it can generate a decrease in adaptive immunity and an increase in innate immunity.

During sleep, the human body acquires specific characteristics such as:

Muscle immobilization and relaxation
Repetitive motions with no apparent function
Slow breathing

These physical and mental characteristics are in an easily reversible state, so the loss of sleep generates a cumulative debt not recoverable (27).

Sleep is the physiological outcome in which it is related to age, attachment, people's habits, mental health, and diseases. About a third of their lives are spent sleeping (28). Humans in their initial stages of life require a high number of hours of sleep ranging from 16 to 18 h. As his life progresses, this requirement decreases until he reaches 6 hours in his old age. Throughout life, sleep contributes to the health of people in which they perform different functions such as:

- Establishment or conservation of energy
- Elimination of free radicals accumulated during the day
- Thermal regulation
- Metabolic and endocrine regulation
- Sympathetic homeostasis
- Immune activation
- Memory consolidation (27)

Taking into account all these aspects, poor sleep is synonymous with pathologies such as cardiovascular, type II diabetes mellitus, metabolic syndrome, psychiatric diseases and cancer (28). Therefore, sleep is considered as a behavior that is characterized by the urgent need to sleep, encourages us to look for a comfortable, warm and quiet place to lie down and stay there for several hours (29).

Sleep phases

Sleep is not a homogeneous process, in fact, there are two types of sleep that act cyclically and with a duration of 90 min, which are: non-REM sleep and continues with REM sleep.

Non-rem sleep consists of 4 phases: (19)

Stage I: Drowsiness

The stage of drowsiness occurs when there is a transition between fast and low amplitude waves also called alpha waves to high amplitude slow waves called theta. When this happens, people gradually begin to disconnect their interaction with the environment and their thinking wanders. (30).

Stage II: Mild sleepiness

At this stage, sleep spindles and k complexes may be present. The first constitute rafas of fast waves for a time between 2 to 5 min, on the other hand, the k complexes are broad and sharp waves that occur for an interval of 1 min, both are characteristic of this stage. For this time people have greater muscle relaxation, disconnection with the environment which can be reversed under the influence of a strong stimulus and finally a progressive decline in their metabolic rate (30)

Stage III: moderate to deep sleep

Stage IV: Deeper level of sleep

Both stages III and IV are part of the longer and deeper sleep, it is significantly restorative in which slow waves occur is here where people can rest. Additionally, your metabolic rate decreases to the maximum along with your connection and reaction to the environment. It should be noted that people

who are at this stage are more difficult to lift and if they achieve it, they present confusion that only lasts a certain period of time (30).

On the other hand, REM sleep (rapid eye movement sleep) or paradoxical sleep stands out for its dream phase where the brain produces images or events that originate while sleeping. (19). This phenomenon is known as dreaming and can be reported in a proportion of 80% after the awakening of an individual, which is why dreaming does not represent a lack of life or mental activity, additionally these dreams in the REM phase are cinematographic and in color (31). This phase usually occupies a time interval between 20 and 30 min. In addition, in order to avoid injuries there is a decrease in muscle activity (19).

In the first half of the night, phases III and IV of non-REM sleep develop, while the second part develops the longer periods of REM sleep. (19). At this stage people try to reach a state of wakefulness, not reaching phase I enters another different type of sleep which is represented by patterns similar to those of the stage. During this stage there is great difficulty in waking the individual and the rate of metabolic activity and connectivity with the environment are significantly accelerated, added to the repetitive movement of the eyes. This stage is known as paradoxical sleep, it can also present sudden jerks, irregular heart and respiratory rate and in case of men there may be erections (30).

Melatonin in the sleep cycle

All physiological functions are regulated according to the secretory cycles of molecular messengers, which are regulated by rhythms dependent on light or darkness, several hormones are generated following the circadian rhythm of sleep (14).

When there is no light, melatonin is constantly being secreted, which encourages people to sleep. The endocrine system is responsible for controlling the concentration of melatonin, with the first secretion around 10 pm and another after that helps maintain sleep control at 2 am (14). Melatonin is a compound synthesized by several extra-pineal and non-endocrine organs such as the retina, skin, bone marrow, serotonin-producing cells of the gastro-intestinal tract, cerebellum and immune system. Melatonin is regulated by the suprachiasmatic nucleus and regulates SCN and peripheral clocks throughout the body, making it a marker of circadian rhythms. For its synthesis, the cells of the pineal gland collect tryptophan from the blood and through hydroxylation and decarboxylation reactions converts it into serotonin later into N-acetylserotonin then into methylated and finally into melatonin. (32). Additionally, the hypothalamus sends signals that result in the reduction of body temperature facilitating the resting state (14).

The blue light emitted by the screens of digital and electronic devices can delay the release of melatonin, increase alertness and reset the body's internal clock to a later time. The reason is because wavelength affects melatonin levels more than any other wave. People who come into contact with blue light devices frequently and at night, have a harder time falling asleep, have fewer REM dreams, and wake up sleepier even after eight hours of sleep (11). Among the diseases caused by the suppression of melatonin synthesis are high blood pressure, sleep disorder, cardiovascular disease and some type of cancer (33).

Chrono interruption

It is the interruption of the circadian cycle and refers to a long-term deterioration of the physiological and biochemical rhythms of the organism, which can trigger different pathologies (14). These interruptions can be due either to eating or sleeping at unusual hours, these chrono-disruptors are agents or stimuli, which can be endogenous or exogenous. These are capable of altering the temporal organization of physiological functions and their hierarchy, establish an order within the functional organization of the organism, but in excess act as chrono-disruptors. Chrono-disruption or chrono-disruption can also produce alterations in the genes of the biological clock and is usually manifested more frequently by sleep disorders (34).

Diseases related to the malfunction of the biological clock can be classified into two groups according to their relationship with the circadian system (19). Here's how they are:

Directly related: these pathologies affect the machinery of the biological clock therefore patients will have an abnormal circadian rhythm being more appreciable their wake and sleep cycle (19).

Indirectly related: are those that are associated with mental disorders, metabolic, cancer, immune problems, asthma or rheumatoid arthritis.

The different circadian rhythms are altered in the same way in some neurodegenerative diseases in which different areas of the brain are damaged, so this chrono-disruption would not only be a symptom of these diseases but can also modify the evolution and progression (35).

Circadian sleep disorder

Humans have endogenous circadian cycles, such that, depending on activity, rest, sleep and awakening can have several variations called chronotypes. The chronotypes can be differentiated into morning and evening. In case of morning chronotypes produce that people wake up early and are more alert with high work capacity and exercise in the morning. On the other hand, an evening chronotype is characterized by causing people to sleep and wake up later. These chronotypes have an influence on habits and induce metabolic adaptations, usually the population is at a standstill between the two. (36).

Circadian cycles vary from person to person and are codependent on circadian rhythm synchronization. However, there are differences with respect to the schedule, which allows to distinguish between normal and pathological. Pathological circadian cycles are classified into:

Primary disorders:

1. Delayed sleep phase syndrome: characteristic that sleep and awakening have a delay between 2 or more hours in the socially accepted schedule. What 6 to 16% of the population suffers
2. Sleep phase advancement syndrome: Sleep and wake times are ahead of the socially accepted schedule
3. Irregular sleep rhythm: in this case the sleep and wake cycles are indefinite so that people who suffer from it can sleep several times a day and for short periods and is related to dementia, neurological problems and intellectual disability
4. Free sleep rhythms: it is the product of the desynchronization of the clock with the light-dark cycle, usually present in people with visual impairment where the circadian cycle is greater and is delayed every day.

Secondary disorders: are those caused by external stimuli such as the use of medications or drugs such as:

1. Jet lag: they are generated by the change of schedule in a trip and occur one or two days later and last a maximum of one week.
2. Shift work disorder: it takes place in people with overnight work and is associated with pathologies such as: neurodegenerative diseases, diabetes, hypertension, among others (19).

Taking into account these types of disorders, it must be embroidered that if a person has a chronic sleep deficit may present other types of affectations such as (37).

In sleep and cognition, not all areas of this are affected, however, those affected are the maintenance of attention and the speed of thought, which can be reversed by resuming the respective hours of sleep

In sleep and mental health, sleep plays a very important role in improving emotional, social and behavioral quality.

In sleep and physical health, they have been linked to obesity, cardiometabolic markers, type I diabetes, asthma, headaches, migraines.

On the other hand in people with problems of excessive sleepiness, which is the product of insufficient or inadequate sleep may present (37):

- Obstructive sleep apnea
- Narcolepsy

- S. of restless legs
- Movement disturbances
- Psychiatric illnesses
- Use of caffeine, narcotic substances and alcohol (37)

Light is an electromagnetic radiation that allows illumination and therefore keeps things visible. Light can be emitted by natural sources, such as the sun or flame, and by artificial sources such as lamps and light bulbs (38).

For living beings, light is one of the most used physical signals to regulate their metabolic processes. In fact, most cells follow the light-dark cycle so that it is considered essential for the development of the life cycle. For example, humans are able to synthesize vitamin D from lipid molecules because ultraviolet B (UvB) light is able to penetrate the dermis and epidermis and change the chemical structure of cholesterol-derived molecules (39). In the same way, light is able to regulate circadian cycles since the fluctuation of light in 24 hours compromises both peripheral and central oscillators, which transmit the information generating multiple physiological and behavioral responses (40).

The rapid advancement of science and technology has developed in such a way that the social, work and academic life of human beings is dependent on artificial light, therefore, there is no longer the natural cycle of light and darkness that provides day and night (15). In fact, during the last 20 years there have been multiple studies that conclude that the Blue light, emitted by digital devices, has the ability to affect the circadian cycle since it reduces melatonin secretion and therefore circulating melatonin levels (41).

This allows us to determine that the constant and considerable use of digital devices that emit blue light before sleep do produce alterations in the circadian cycle. The reason is that the wavelength of blue light generates a greater effect on the waking state, thus affecting the quality of people's sleep (11). This is because the natural processes of the body such as cognitive and physical exercise that require a high metabolic and energy value are performed in the daytime, while the processes of consolidation, repair and regeneration of the cell phone occur mostly at night. For this reason, exposure to blue light, i.e., a short wavelength, at night represses the various natural nocturnal processes in order to increase alertness. As a result, various alterations and diseases such as metabolic problems, depression, anxiety, eye irritation, headaches memory and learning deficiency develop (40).

Since human nature is social and physiological, the study of how the artificial emission of blue light affects people's lifestyles is essential (15). In fact, the evidence of the impact of blue light on humans is vast, not only reaching to impact on physical health but also on the behavior and attitude of people (15). Finally, it is suggested to look for qualitative and quantitative research spaces in which this topic is studied in more detail.

4. Conclusion

The circadian cycle comprises various processes in the body and is regulated by different factors such as blue light, which at greater exposure at night prevents the segregation of melatonin in the body thus increasing lack of sleep and wakefulness therefore decrease the hours of sleep affecting the state of physical and mental health influencing the quality of life.

In recent times, artificial light has significantly influenced the circadian cycle since previously people did not suffer from the various sleep disorders, it has even been shown that the short wavelength of artificial light promotes alertness, on the contrary, the long wavelength of natural light does not have much incidence on the waking state.

The alterations of the circadian cycle cause various sleep disorders which in turn directly influence the state of health causing different conditions such as obesity, anxiety, insomnia, depression, eye fatigue among others. Therefore, maintaining a correct regulation of the circadian cycle can improve the quality of life.

It is important that the biological clock is synchronized to reduce the negative repercussions on the state of health, however, by using a constant daily schedule and adapted to the hours of light and darkness to improve the state of physical and mental health of people.

Scientific advances in the circadian cycle have provided a lot of information, however, due to the development of genetics it has been shown that there are various circadian mechanisms that are not fully clarified, so it is an area open to new research in order to improve human health.

References:

1. Ashton A, Foster R, Jagannath A. (2022). Photic Entrainment of the Circadian System. *International Journal of Molecular Sciences*, 23(2), 729. DOI: [Link](#)
2. Dibner C, Schibler U, Albrecht U. (2010). The mammalian circadian timing system: organization and coordination of central and peripheral clocks. *Annual Review of Physiology*, 72, 517-549. DOI: [Link](#)
3. Porth. (2019). *Pathophysiology Health Disorders: Basics* (10th ed.). Madrid: Medica Panamericana.
4. Cain SW, McGlashan EM, Vidafar P, Mustafovska J, Curran SPN, Wang X, et al. (2020). Evening home lighting adversely impacts the circadian system and sleep. *Scientific Reports*, 10(1), 19110. DOI: [Link](#)
5. Guerrero-Vargas NN, Ángeles-Castellanos M, Escobar Briones C. (2018). The adverse effects of artificial light at night. *Revista Digital Universitaria*, 19(3). [Link](#)
6. Phillips AJK, Vidafar P, Burns AC, McGlashan EM, Anderson C, Rajaratnam SMW, et al. (2019). High sensitivity and interindividual variability in the response of the human circadian system to evening light. *Proceedings of the National Academy of Sciences*, 116(24), 12019-12024. DOI: [Link](#)
7. Faizin MN, Wahyuningrum E, Gayatina AK. (2021). Relationship Between Smartphone Addiction and Sleep Disturbance in School Age Children. *Jurnal Ilmu Keperawatan Jiwa*, 4(4), 733-740.
8. Lazzarini Ospri L, Prusky G, Hattar S. (2017). Mood, the Circadian System, and Melanopsin Retinal Ganglion Cells. *Annual Review of Neuroscience*, 40(1), 539-556. DOI: [Link](#)
9. Zambrano V, Jeannine R. (2020). Effect of blue light from digital devices on the sleep cycle of young patients, 125.
10. Partch CL, Green CB, Takahashi JS. (2014). Molecular architecture of the mammalian circadian clock. *Trends in Cell Biology*, 24(2), 90-99. DOI: [Link](#)
11. Trujillo Silva AM. (2019). Study of the incidence of blue light on the circadian cycle in young people of higher education in the northern sector of the metropolitan district of Quito period 2019. Prevention program in the use of electronic devices for university students. [Link](#)
12. Lowrey PL, Takahashi JS. (2004). Mammalian circadian biology: Elucidating Genome-Wide Levels of Temporal Organization. *Annual Review of Genomics and Human Genetics*, 5(1), 407-441. DOI: [Link](#)
13. Dibner C, Schibler U, Albrecht U. (2010). The Mammalian Circadian Timing System: Organization and Coordination of Central and Peripheral Clocks. *Annual Review of Physiology*, 72(1), 517-549. DOI: [Link](#)
14. Millán Arroyo C. (2017). Effects of blue light on the circadian rhythm of sleep. [Link](#)
15. Farhud D, Aryan Z. (2018). Circadian Rhythm, Lifestyle and Health: A Narrative Review. *Iranian Journal of Public Health*, 47(8), 1068-1076.
16. Sliney DH. (2016). What is light? The visible spectrum and beyond. *Eye*, 30(2), 222-229. DOI: <https://doi.org/10.1038/eye.2015.276>
17. Ilie AM. (2021). Influence of light on waking states and pupillary tone. [Link](#)
18. Roenneberg T, Mrosovsky M. (2002). Light Reception: Discovering the Clock-Eye in Mammals. *Current Biology*, 12(5), R163-R165.
19. Galán LC. (2019). Biological clock and circadian rhythm.
20. Ko. (2020). Circadian regulation in the retina: From molecules to network. *European Journal of Neuroscience*, 51(1), 194-216. DOI: <https://doi.org/10.1111/ejn.14150>
21. Tähkämö L, Partonen T, Pesonen AK. (2019). Systematic review of light exposure impact on human circadian rhythm. *Frontiers in Neurology*, 10, 803. DOI: <https://doi.org/10.3389/fneur.2019.00803>
22. Salmerón EJ. (2022). Blue light: dangers and benefits. *Archivos de la Sociedad Española de Oftalmología*, 97(7), 408-415. DOI: <https://doi.org/10.1016/j.oftal.2021.10.003>
23. Catalán RM. (2018). Spectrophotometric characterization of contact lenses and ophthalmic lenses. [Link](#)
24. González Raúl, Guamán A, Vidal del Río MM. (2021). BLUE AND ULTRAVIOLET LIGHT AS AN OCULAR RISK FACTOR. *Rev UNIANDES Health Sciences*, 4(3), 10. DOI: <https://doi.org/10.35707/RUCS.V4N3.52>
25. Redondo L. (2020). Blue light filters: spectral characterization and analysis of their use. [Link](#)
26. Rico-Rosillo MG, Vega-Robledo GB. (2018). Sleep and immune system. *Revista Alergia Mexico*, 65(2), 160-170. DOI: <https://doi.org/10.29262/RAM.V65I2.368>
27. Lira D, Custodio N. (2018). Sleep disorders and their complex relationship with cognitive functions. *Revista de Neuropsiquiatría*, 81(1), 20-30. DOI: <https://doi.org/10.20453/RNP.V81I1.3342>
28. Fabres L, Moya P. (2021). Dream: General concepts and their relationship with quality of life. *Revista Médica de Chile*, 149(5), 743-749. DOI: <https://doi.org/10.4067/S0034-98872021000500743>
29. Bolaños J, Huertas M. (2021). Management and updated treatment of the most frequent sleep disorders: a daily review. *Acta Médica Costarricense*, 63(3), 103-111.

30. Benavides-Endara P, Ramos-Galarza C, Benavides-Endara P, Ramos-Galarza C. (2019). Neurobiological foundations of sleep. *Revista Ecuatoriana de Neurología*, 28(3), 73-80.
31. Velayos J, Moleres F, Irujo A, Yllanes D, Paternain B. (2007). Anatomical bases of sleep. *Neurology*, 30(1), 7-17. DOI: [https://doi.org/10.1016/S0213-4853\(07\)71547-3](https://doi.org/10.1016/S0213-4853(07)71547-3)
32. Poza JJ, Pujol M, Ortega-Albás JJ, Romero O. (2022). Melatonin in sleep disorders. *Neurology*, 37(7), 575-585. DOI: <https://doi.org/10.1016/J.NRL.2021.06.001>
33. Santisteban M, Santisteban M. (2019). Healthy sleep habits, melatonin and breast cancer. *Anales del Sistema Sanitario de Navarra*, 42(2), 245-248. DOI: <https://doi.org/10.23938/ASSN.0745>
34. Ursa A, Ursa MI. (2020). Affections due to chronodisruption. Preventive and curative measures. *Naturopathic Medicine*, 14(1). [Link](#)
35. Madrid Navarro CJ. (2018). Circadian rhythms and chronodisruption in Parkinson's disease. [Link](#)
36. Madrid J, Pin Arboledas G, Ferrández Gomariz M. (2018). Functional organization of the human circadian system. Development of the circadian rhythm in the child. Alterations of the wake-sleep rhythm. Phase delay syndrome. *Integral Pediatric*, XXII(8), 385-395.
37. Pin-Groves G. (2020). Sleep and its problems, how to address them? *Revista Pediatría Atenas Primaria*, 22(85), 11-24. DOI: <https://doi.org/10.1016/J.RPAT.2019.04.001>
38. Sliney DH. (2016). What is light? The visible spectrum and beyond. *Eye*, 30(2), 222-229. DOI: <https://doi.org/10.1038/EYE.2015.254>
39. Holick MF. (2008). Sunlight, UV-radiation, vitamin D and skin cancer: how much sunlight do we need? *Advances in Experimental Medicine and Biology*, 624, 1-15. DOI: https://doi.org/10.1007/978-0-387-77574-6_1
40. Yamanaka Y. (2020). Basic concepts and unique features of human circadian rhythms: implications for human health. *Nutrition Reviews*, 78(Supplement_3), 91-96. DOI: <https://doi.org/10.1093/NUTRIT/NUAA075>
41. Thapan K, Arendt J, Skene DJ. (2001). An action spectrum for melatonin suppression: evidence for a novel non-rod, non-cone photoreceptor system in humans. *Journal of Physiology*, 535(1), 261-267. DOI: <https://doi.org/10.1111/J.1469-7793.2001.00261.x>
42. Barrero RA, Hernández YS, Pravia MP. (2020). Key dimensions of effective public management in local governments. Application in a case study. *University and Society*, 12(6), 411-420. DOI: <https://rus.ucf.edu/cu/index.php/rus/article/view/1863>
43. Ayala JMB, Cando JLM, Gallegos SBG. (2020). Analysis of the principle of concurrence in the electronic reverse auction in the Santo Domingo canton using Pestel analysis combined with Satty's AHP. *University and Society*, 12(6), 366-372. DOI: <https://rus.ucf.edu/cu/index.php/rus/article/view/1856>
44. Moncayo JCN, Giler SAM, WAC Street. (2020). Legal logic, a substantial tool for understanding the relationship between the state and law. *University and Society*, 12(6), 437-443. DOI: <https://rus.ucf.edu/cu/index.php/rus/article/view/1870>
45. Leyva Vázquez MY, Viteri Moya JR, Estupiñán Ricardo J, Hernández Cevallos RE. (2021). Diagnosis of the challenges of post-pandemic scientific research in Ecuador. *Contemporary Dilemmas: Education, Politics and Value*, 9(SPE1). [Link](#).
46. Ricardo, J. E., Vásquez, Á. B. M., Herrera, R. A. A., Álvarez, A. E. V., Jara, J. I. E., & Hernández, N. B. (2018). Management System of Higher Education in Ecuador: Impact on the Learning Process. *Contemporary Dilemmas: Education, Politics and Value*, (Special). [ProQuest Link](#)
47. Gómez, G. A. Á., Vázquez, M. Y. L., & Ricardo, J. E. (2022). Application of Neutrosophy to the Analysis of Open Government, Its Implementation, and Contribution to the Ecuadorian Judicial System. *NSS*, 52, 215-224. [Link](#)
48. Tapia, M. E. Á., Salcedo, V. H. L., & Narváez, M. V. C. (2020). Denunciation of ICSID Investment Treaties: I/A Court H.R., Case of Bolivia, Ecuador, and Venezuela. *University and Society*, 12(6), 386-393. [Link](#)
49. Arias, N. G., Palacios, T. H. C., & Paronyan, H. (2020). The "Empty Chair": Its Use by Young People in the Province of Santo Domingo de los Tsáchilas. *University and Society*, 12(6), 462-467. [Link](#)
50. Arias, I. F. B., Manzo, A. D. M., & Piza, I. A. C. (2020). Assessment of the Sanction for Environmental Damage in the Province of Los Ríos. *University and Society*, 12(6), 339-347. [Link](#)