

Immune system

Medical Studies on Melatonin and the Immune system



A strong immune system is an essential factor in human health, because it helps to successfully fight viruses, bacteria and other micro-organisms, making it an important provider of protection against pathogens. It also affects wound healing and plays a key role in protecting against other diseases such as cancer. Melatonin is capable of regulating this complex system in such a way that it offers perfect protection while also not reacting excessively. To this end, it regulates both anti-inflammatory and pro-inflammatory factors, which in turn control immune cells.

Versatile protective mechanisms

Oxidative damage in particular has a severe impact on human health and has been identified as a key factor in the genesis and development of numerous diseases. Melatonin plays a key role in this context. As a natural antioxidant of the body, it offers important protection against free radicals, but it also has many indirect effects too. For example, melatonin activates anti-oxidative enzymes, providing support for DNA repair processes, among other things.

Melatonin reduces cell damage

As was recently confirmed by a study, melatonin is a highly effective agent for treating inflammatory and immune diseases by inhibiting toll-like receptors (TLRs). These are of fundamental importance in the pathophysiology of diseases associated with inflammation processes, including those related to neurodegenerative disorders and cancer. Other pro-inflammatory and anti-inflammatory factors are also positively affected by melatonin.

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Melatonin as adjuvant treatment for coronavirus disease 2019 pneumonia patients requiring hospitalization (MAC-19 PRO): a case series

2020-06 Castillo RR, Quizon GRA, Juco MJM, Roman ADE, de Leon DG, Punzalan FER, Guingon RBL, Morales DD, Tan DX, Reiter RJ

Treatment for coronavirus disease 2019 (COVID19) pneumonia remains empirical and the search for therapies that can improve outcomes continues. Melatonin has been shown to have anti-inflammatory, antioxidant, and immune-modulating effects that may address key pathophysiologic mechanisms in the development and progression of acute respiratory distress syndrome (ARDS), which has been implicated as the likely cause of death in COVID19.

Melatonin Inhibits COVID-19-induced Cytokine Storm by Reversing Aerobic Glycolysis in Immune Cells: A Mechanistic Analysis

2020-06

Reiter RJ, Sharma R, Ma Q, Dominquez-Rodriguez A, Marik PE, Abreu-Gonzalez P

The pathogenesis of a COVID-19 respiratory infection, in a major way, is related to what is referred to as the cytokine storm [cytokine storm syndrome (CSS, hypercytokinemia, etc.)], i.e., it is a hyper-inflammatory response.

Therapeutic Algorithm for Use of Melatonin in Patients With COVID-19

2020-05

Reiter RJ, Abreu-Gonzalez P, Marik PE, Dominguez-Rodriguez A

The coronavirus, COVID-19, has infected hundreds of thousands and killed tens of thousands of individuals worldwide. This highly infectious condition continues to ravage the world population and has yet to reach its peak infective rate in some countries.

The Effects of Melatonin Supplementation on Parameters of Mental Health, Glycemic Control, Markers of Cardiometabolic Risk, and Oxidative Stress in Diabetic Hemodialysis Patients: A Randomized, Double-Blind, Placebo-Controlled Trial.

2020-05

Ostadmohammadi V, Soleimani A, Bahmani F, Aghadavod E, Ramezani R, Reiter RJ, Mansournia MA, Banikazemi Z, Soleimani M, Zaroudi M, Asemi Z

This study evaluated the effects of melatonin supplementation on parameters of mental health, glycemic control, markers of cardiometabolic risk, and oxidative stress in diabetic hemodialysis (HD) patients.

Effect of Nocturnal Melatonin Intake on Cellular Damage and Recovery From Repeated Sprint Performance During an Intensive Training Schedule.

2020-05

Farjallah MA, Ghattassi K, Ben Mahmoud L, Graja A, Boudaya M, Elleuch H, Jammoussi K, Sahnoun Z, Souissi N, Chtourou H, Hammouda O

An optimal recovery between training sessions is of similar if not greater importance as the training content and program of the training, itself. One of the most used strategies for

improving recovery is the ingestion of supplements.

Network-based Drug Repurposing for Human Coronavirus.

2020-04 Zhou Y, Hou Y, Shen J, Huang Y, Martin W, Cheng F

Human Coronaviruses (HCoVs), including severe acute respiratory syndrome coronavirus (SARS-CoV), Middle east respiratory syndrome coronavirus (MERS-CoV), and 2019 novel coronavirus (2019-nCoV), lead global epidemics with high morbidity and mortality. However, there are currently no effective drugs targeting 2019-nCoV.

COVID-19: Melatonin as a potential adjuvant treatment.

2020-04 Zhang R, Wang X, Ni L, Di X, Ma B, Niu S, Liu C, Reiter RJ

This article summarizes the likely benefits of melatonin in the attenuation of COVID-19 based on its putative pathogenesis.

Can melatonin reduce the severity of COVID-19 pandemic?

2020-04 Shneider A, Kudriavtsev A, Vakhrusheva A

The current COVID-19 pandemic is one of the most devastating events in recent history. The virus causes relatively minor damage to young, healthy populations, imposing life-threatening danger to the elderly and people with diseases of chronic inflammation. Therefore, if we could reduce the risk for vulnerable populations, it would make the COVID-19 pandemic more similar to other typical outbreaks.

Melatonin in Mitochondria: Mitigating Clear and Present Dangers.

2020-04 Reiter RJ, Ma Q, Sharma R

In cancer cells, glucose is primarily metabolized to pyruvate and then to lactate in the cytosol.

Treatment of Ebola and other infectious diseases: melatonin “goes viral”.

2020-04 Reiter RJ, Sharma R

This review summarizes published reports on the utility of melatonin as a treatment for virus-mediated diseases. Of special note are the data related to the role of melatonin in influencing Ebola virus disease.

Daily and seasonal mitochondrial protection: Unraveling common possible mechanisms involving vitamin D and melatonin.

2020-04 Mocayar Marón FJ, Ferder L, Reiter RJ, Manucha W

From an evolutionary point of view, vitamin D and melatonin appeared very early and share functions related to defense mechanisms. In the current clinical setting, vitamin D is exclusively associated with phosphocalcic metabolism. Meanwhile, melatonin has chronobiological effects and influences the sleep-wake cycle.

PAK1-blockers: Potential Therapeutics against COVID-19.

2020-04 Maruta H, He H

PAK1 (RAC/CDC42-activated kinase 1) is the major "pathogenic" kinase whose abnormal activation causes a wide variety of diseases/disorders including cancers, inflammation, malaria and pandemic viral infection including influenza, HIV and COVID-19.

Melatonin: Roles in influenza, Covid-19, and other viral infections.

2020-04 Anderson G, Reiter RJ

There is a growing appreciation that the regulation of the melatonergic pathways, both pineal and systemic, may be an important aspect in how viruses drive the cellular changes that underpin their control of cellular function.

Daytime melatonin levels in saliva are associated with inflammatory markers and anxiety disorders.

2020-02 Sundberg I, Rasmusson AJ, Ramklint M, Just D, Ekselius L, Cunningham JL

The bidirectional interaction between melatonin and the immune system has largely gone unexplored in a clinical context and especially in a psychiatric population. This study explored the association between melatonin during the day and inflammatory cytokines in young adult patients seeking psychiatric care.

Melatonin and Parkinson Disease: Current Status and Future Perspectives for Molecular Mechanisms.

2020-01 Tamtaji OR, Reiter RJ, Alipoor R, Dadgostar E, Kouchaki E, Asemi Z

Parkinson disease (PD) is a chronic and neurodegenerative disease with motor and nonmotor symptoms. Multiple pathways are involved in the pathophysiology of PD, including apoptosis, autophagy, oxidative stress, inflammation, α -synuclein aggregation, and changes in the neurotransmitters.

Mitochondria: the birth place, battle ground and the site of melatonin metabolism cells.

2019-12 Tan DX, Reiter RJ

It was a surprising discovery when mitochondria, as the power houses of cells, were also found to synthesize the potent mitochondrial targeted antioxidant, melatonin. The melatonin synthetic enzyme serotonin N-acetyltransferase (SNAT) was found in matrix and also in the intermembrane space of mitochondria.

Melatonin and its ubiquitous anticancer effects.

2019-12 Bhattacharya S, Patel KK, Dehari D, Agrawal AK, Singh S

Melatonin (N-acetyl-5-methoxy-tryptamine), which is generally considered as pleiotropic and multitasking molecule, secretes from pineal gland at night under normal light or dark conditions. Apart from circadian regulations, Melatonin also has antioxidant, anti-ageing, immunomodulation and anticancer properties.

Melatonin has profound effects on mitochondrial dynamics in myocardial ischaemia/reperfusion.

2019-11 Dube K, Dhanabalan K, Salie R, Blignaut M, Huisamen B, Lochner A

Research focus recently shifted to mitochondrial dynamics and the role of fusion and fission in cardioprotection. The aim of this study was to evaluate (i) the function and dynamics of mitochondria isolated from hearts exposed to ischaemia/reperfusion (I/R) (ii) the effects of melatonin, a powerful cardioprotectant, on mitochondrial dynamics in I/R.

Infusion of Melatonin Into the Paraventricular Nucleus Ameliorates Myocardial Ischemia-Reperfusion Injury by Regulating Oxidative Stress and Inflammatory Cytokines.

2019-10 Yang JB, Kang YM, Zhang C, Yu XJ, Chen WS

Melatonin, the receptors for which are abundant in the hypothalamic paraventricular nucleus (PVN), can protect the heart from myocardial ischemia-reperfusion (MI/R) injury. The aim of this study was to determine whether the infusion of melatonin into the PVN protects the heart from MI/R injury by suppressing oxidative stress or regulating the balance between proinflammatory cytokines and anti-inflammatory cytokines in MI/R rats.

The Neuroprotective Effects of Melatonin: Possible Role in the Pathophysiology of Neuropsychiatric Disease.

2019-10 Lee JG, Woo YS, Park SW, Seog DH, Seo MK, Bahk WM

Melatonin is a hormone that is secreted by the pineal gland. To date, melatonin is known to regulate the sleep cycle by controlling the circadian rhythm. However, recent advances in neuroscience and molecular biology have led to the discovery of new actions and effects of melatonin.

Melatonin and (-)-Epigallocatechin-3-Gallate: Partners in Fighting Cancer.

2019-07 Zhang L, He Y, Wu X, Zhao G, Zhang K, Yang CS, Reiter RJ, Zhang J

We have demonstrated previously that melatonin attenuates hepatotoxicity triggered by high doses of (-)-epigallocatechin-3-gallate (EGCG) in mice. The current work investigated the influence of melatonin on the oncostatic activity of EGCG in two cancer cell lines, wherein melatonin induced an opposite response of p21.

Co-administering Melatonin With an Estradiol-Progesterone Menopausal Hormone Therapy Represses Mammary Cancer Development in a Mouse Model of HER2-Positive Breast Cancer.

2019-07 Dodda BR, Bondi CD, Hasan M, Clafshenkel WP, Gallagher KM, Kotlarczyk MP, Sethi S, Buszko E, Latimer JJ, Cline JM, Witt-Enderby PA, Davis VL

Melatonin has numerous anti-cancer properties reported to influence cancer initiation, promotion, and metastasis. With the need for effective hormone therapies (HT) to treat

menopausal symptoms without increasing breast cancer risk, co-administration of nocturnal melatonin with a natural, low-dose HT was evaluated in mice that develop primary and metastatic mammary cancer.

Melatonin, a toll-like receptor inhibitor: Current status and future perspectives.

2019-06 Tamtaji OR, Mobini M, Reiter RJ, Azami A, Gholami MS, Asemi Z

Toll-like receptors (TLRs) are crucial activators of inflammatory responses, they are considered immune receptors.

Chronodisruption, Metabolic Homeostasis, and the Regulation of Inflammation in Adipose Tissues.

2019-06 Kolbe I, Oster H

Molecular circadian clocks align daily behavioral and metabolic rhythms with the external day-night cycle. Priming energy metabolism for recurring changes on a 24-hour basis, these clocks are deeply interlinked with metabolic homeostasis and health.

Melatonin and pancreatic cancer: Current knowledge and future perspectives.

2019-05 Tamtaji OR, Mirhosseini N, Reiter RJ, Behnamfar M, Asemi Z

Pancreatic cancer has a high mortality rate due to the absence of early symptoms and subsequent late diagnosis; additionally, pancreatic cancer has a high resistance to radio- and chemotherapy. Multiple inflammatory pathways are involved in the pathophysiology of pancreatic cancer.

Melatonin and non-small cell lung cancer: new insights into signaling pathways.

2019-05 Pourhanifeh MH, Sharifi M, Reiter RJ, Davoodabadi A, Asemi Z

Non-small-cell lung cancer (NSCLC) is a type of malignancy with progressive metastasis having poor prognosis and lowered survival resulting from late diagnosis. The therapeutic approaches for the treatment of this incurable cancer are chemo- and radiotherapy.

Melatonin is a potential inhibitor of ovarian cancer: molecular aspects.

2019-03 Zare H, Shafabakhsh R, Reiter RJ, Asemi Z

Ovarian cancer is one of the most common causes of morbidity related to gynecologic malignancies. Possible risk factors are including hereditary ovarian cancer, obesity, diabetes mellitus, alcohol consumption, aging, and smoking.

Night workers have lower levels of antioxidant defenses and higher levels of oxidative stress damage when compared to day workers.

2019-03 Teixeira KRC, Dos Santos CP, de Medeiros LA, Mendes JA, Cunha TM, De Angelis K, Penha-Silva N, de Oliveira EP, Crispim CA

The effects of circadian misalignment and work shift on oxidative stress profile of shift workers have not been explored in the literature. The present study aimed to evaluate the role of shift work (day and night) and social jetlag – a measure of circadian misalignment – with oxidative stress markers.

Aging, Melatonin, and the Pro- and Anti-Inflammatory Networks.

2019-03 Hardeland R

Aging and various age-related diseases are associated with reductions in melatonin secretion, proinflammatory changes in the immune system, a deteriorating circadian system, and reductions in sirtuin-1 (SIRT1) activity.

Melatonin in Heart Failure: A Promising Therapeutic Strategy?

2018-07 Nduhirabandi F, Maarman GJ

Heart failure is a multifactorial clinical syndrome characterized by the inability of the heart to pump sufficient blood to the body. Despite recent advances in medical management, poor outcomes in patients with heart failure remain very high. This highlights a need for novel paradigms for effective, preventive and curative strategies.

Mechanisms Underlying Tumor Suppressive Properties of Melatonin.

2018-07 Bondy SC, Campbell A

There is considerable evidence that melatonin may be of use in the prevention and treatment of cancer. This manuscript will review some of the human, animal and cellular studies that provide evidence that melatonin has oncostatic properties.

Melatonin: A Versatile Protector against Oxidative DNA Damage.

2018-02 Galano A, Tan DX, Reiter RJ

Oxidative damage to DNA has important implications for human health and has been identified as a key factor in the onset and development of numerous diseases. Thus, it is evident that preventing DNA from oxidative damage is crucial for humans and for any living organism. Melatonin is an astonishingly versatile molecule in this context.

Melatonin as a mitochondria-targeted antioxidant: one of evolution's best ideas.

2017-11 Reiter RJ, Rosales-Corral S, Tan DX, Jou MJ, Galano A, Xu B

Melatonin is an ancient antioxidant. After its initial development in bacteria, it has been retained throughout evolution such that it may be or may have been present in every species that have existed. Even though it has been maintained throughout evolution during the diversification of species, melatonin's chemical structure has never changed; thus, the melatonin ...

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Melatonin, a Full Service Anti-Cancer Agent: Inhibition of Initiation, Progression and Metastasis.

2017-04 Reiter RJ, Rosales-Corral SA, Tan DX, Acuna-Castroviejo D, Qin L, Yang SF, Xu K

There is highly credible evidence that melatonin mitigates cancer at the initiation, progression and metastasis phases. In many cases, the molecular mechanisms underpinning these inhibitory actions have been proposed. What is rather perplexing, however, is the large number of processes by which melatonin reportedly restrains cancer development and growth.

Melatonin in the oral cavity: physiological and pathological implications.

2015-02**Reiter RJ, Rosales-Corral SA, Liu XY, Acuna-Castroviejo D, Escames G, Tan DX**

The purpose of this article was to summarize what is known about the function of melatonin in the oral cavity.

Ebola virus disease: potential use of melatonin as a treatment.

2014-11**Tan DX, Korkmaz A, Reiter RJ, Manchester LC**

The purpose of this report is to emphasize the potential utility for the use of melatonin in the treatment of individuals who are infected with the Ebola virus.

Melatonin: its possible role in the management of viral infections – a brief review.

2013-10**Silvestri M, Rossi GA**

Melatonin, a versatile molecule, is synthesized by the pineal gland but also by other organs, including gastrointestinal tract, retina, thymus, bone marrow, and by leukocytes.

On the free radical scavenging activities of melatonin's metabolites, AFMK and AMK.

2013-04**Galano A, Tan DX, Reiter RJ**

The reactions of N(1) -acetyl-N(2) -formyl-5-methoxykynuramine (AFMK) and N(1) -acetyl-5-methoxykynuramine (AMK) with (\cdot) OH, (\cdot) OOH, and \cdot OOCCl₃ radicals have been studied using the density functional theory.

Melatonin: buffering the immune system.

2013-04**Carrillo-Vico A, Lardone PJ, Alvarez-Sánchez N, Rodríguez-Rodríguez A, Guerrero JM**

Melatonin modulates a wide range of physiological functions with pleiotropic effects on the immune system.

Beneficial actions of melatonin in the management of viral infections: a new use for this “molecular handyman”?

2012-09**Boga JA, Coto-Montes A, Rosales-Corral SA, Tan DX, Reiter RJ**

Melatonin (N-acetyl-5-methoxytryptamine) is a multifunctional signaling molecule that has a variety of important functions. Numerous clinical trials have examined the therapeutic usefulness of melatonin in different fields of medicine.

Melatonin in bacterial and viral infections with focus on sepsis: a review.

2012-01 Srinivasan V, Mohamed M, Kato H

Melatonin is a versatile molecule, synthesized not only by the pineal gland, but also in small amounts by many other organs like retina, gastrointestinal tract, thymus, bone marrow, lymphocytes etc.

Fatigue in medical residents leads to reactivation of herpes virus latency.

2011-12 Uchakin PN, Parish DC, Dane FC, Uchakina ON, Scheetz AP, Agarwal NK, Smith BE

The main objective of this study was to detect fatigue-induced clinical symptoms of immune suppression in medical residents. Samples were collected from the subjects at rest, following the first night (low-stress), and the last night (high-stress) of night float.

Melatonin in septic shock: some recent concepts.

2010-12 Srinivasan V, Pandi-Perumal SR, Spence DW, Kato H, Cardinali DP

Melatonin is a versatile molecule, synthesized not only in the pineal gland, but also in many other organs. Melatonin plays an important physiologic role in sleep and circadian rhythm regulation, immunoregulation, antioxidant and mitochondrial-protective functions, reproductive control, and regulation of mood.

Melatonin: a pleiotropic molecule regulating inflammation.

2010-12 Radogna F, Diederich M, Ghibelli L

Melatonin is a neurohormone produced by the pineal gland that regulates sleep and circadian functions. Melatonin also regulates inflammatory and immune processes acting as both an activator and inhibitor of these responses.

Melatonin signaling and cell protection function.

2010-10 Luchetti F, Canonico B, Betti M, Arcangeletti M, Pilolli F, Piroddi M, Piroddi M, Canesi L, Papa S, Galli F

Besides its well-known regulatory role on circadian rhythm, the pineal gland hormone melatonin has other biological functions and a distinct metabolism in various cell types and peripheral tissues. In different tissues and organs, melatonin has been described to act as a paracrine and also as an intracrine and autocrine agent with overall homeostatic functions and pleiotropic effects that include cell protection and pro-survival factor.

Regression of herpes viral infection symptoms using melatonin and SB-73: comparison with Acyclovir.

2008-05 Nunes Oda S, Pereira Rde S

Infection with Herpes simplex virus type 1 (HSV-1) typically causes lesions of the mouth, face, skin, esophagus, or brain. Herpes simplex virus type 2 (HSV-2) usually causes infections of the genitals, rectum, skin, hands, or meninges.

One molecule, many derivatives: a never-ending interaction of melatonin with reactive oxygen and nitrogen species?

2007-01 Tan DX, Manchester LC, Terron MP, Flores LJ, Reiter RJ

Melatonin is a highly conserved molecule. Its presence can be traced back to ancient photosynthetic prokaryotes. A primitive and primary function of melatonin is that it acts as a receptor-independent free radical scavenger and a broad-spectrum antioxidant.

Antioxidant properties of the melatonin metabolite N1-acetyl-5-methoxykynuramine (AMK): scavenging of free radicals and prevention of protein destruction.

2003-12 Ressmeyer AR, Mayo JC, Zelosko V, Sáinz RM, Tan DX, Poeggeler B, Antolín I, Zsizsik BK, Reiter RJ, Hardeland R

In numerous experimental systems, the neurohormone melatonin has been shown to protect against oxidative stress, an effect which appears to be the result of a combination of different actions. In this study, we have investigated the possible contribution to radical scavenging by substituted kynuramines formed from melatonin via pyrrole ring cleavage.

Melatonin-immune system relationships.

2002-02 Guerrero JM , Reiter RJ

In this paper we review the historical milestones that first highlighted the existence of a relationship between melatonin and the immune system and we summarize data from experiments which correlate the rhythmic production of melatonin with the rhythmic activity of the immune system.

Effects of melatonin treatment in septic newborns.

2001-12 Gitto E, Karbownik M, Reiter RJ, Tan DX, Cuzzocrea S, Chiurazzi P, Cordaro S, Corona G, Trimarchi G, Barberi I

Free radicals have been implicated in the pathogenesis of neonatal sepsis and its complications.



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