



## HOW A COMPONENT OF MARIJUANA CAN BE USED TO TREAT EPILEPSY

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### YOUNG REVIEWERS:



ANYA

AGE: 15



MARINA

AGE: 14

In the past, plants were the only medical resources available to people. Although plants were used a lot, sometimes they had dangerous effects. The evolution of science has allowed us to separate the helpful and dangerous compounds from various plants. An example is *Cannabis sativa*, also known as marijuana or weed, one of the most commonly used recreational drugs worldwide. These plants produce hundreds of compounds, called cannabinoids. The two most famous cannabinoids are tetrahydrocannabinol (THC), which produces the “high” sensation and might cause some of the negative effects of cannabis, and cannabidiol (CBD), which might be useful for treating certain diseases. In this article, we will explain how CBD can be used to treat epilepsy, a disease that affects people’s brain

function. But remember: we are talking about the use of cannabinoids for therapeutic purposes only, not recreational use of marijuana.

## EPILEPSY: A DISORDER OF THE NERVOUS SYSTEM

The human body is an amazing machine, and the nervous system is an important part of it. The nervous system, which contains the brain, spinal cord, and nerves, controls functions that are both under our control, such as thinking and moving, and those that are controlled without thinking about them, like heartbeat and bowel movements.

Imagine that your brain is a school, made up of a team of teachers and students: the neurons. Neurons are an important cell type within the nervous system, and they pass and receive information all the time, controlling many body functions. Teachers and students must talk to each other to exchange information. This process takes place in classrooms. These are the synapses: areas where two neurons meet to communicate. The words spoken are **neurotransmitters**, chemical signals responsible for conversations between neurons. But sometimes everyone tries to communicate at the same time, and the activities in the school go wrong. This happens in the brains of people with **epilepsy**, the most common disease of the nervous system [1].

Epilepsy is a disease in which people's brains sometimes emit incorrect signals, due to the irregular activity of neurons. These signals trigger epileptic seizures, which are characterized by simultaneous and excessive neuron activity in the brain (Figure 1) [1]. Epilepsy may have several causes, including lack of oxygen in the brain during childbirth, problems with metabolism or the immune system, high fever, a strong blow to the head, infections, and even the presence of certain genes. Intense emotions, specific noises, odors, lights, alcohol intake, or sleep deprivation can trigger seizures in people who suffer from epilepsy [1].

The incorrect neuron signaling in epilepsy may occur in one or many regions of the brain. For example, it can affect the frontal lobe (behind the forehead), triggering uncoordinated movements. It can affect the temporal lobes (the left and right sides of the brain), which process emotions and are important for short-term memory. In the parietal lobe (top of the head), incorrect signaling can cause sensory changes. And, in the occipital lobe (back of the head), improper signaling can generate visual changes. In most cases, seizures also result in a temporary loss of consciousness.

Epilepsy is a treatable disease, but 30% of epilepsy patients do not respond well to common treatments [2]. Therefore, new treatment

### NEURO-TRANSMITTERS

Signaling molecules produced by neurons. Through them it is possible to send information to other cells.

### EPILEPSY

A neurological disorder that affects the activity of neurons in the brain and causes seizures.

### Figure 1

Epileptic seizures are caused by excessive and simultaneous neuron activity in the brain—like everyone talking at once in a classroom. Symptoms of epileptic seizures can include increased salivation, uncoordinated movements, loss of control over bodily functions (like peeing or pooping) and temporary loss of consciousness.

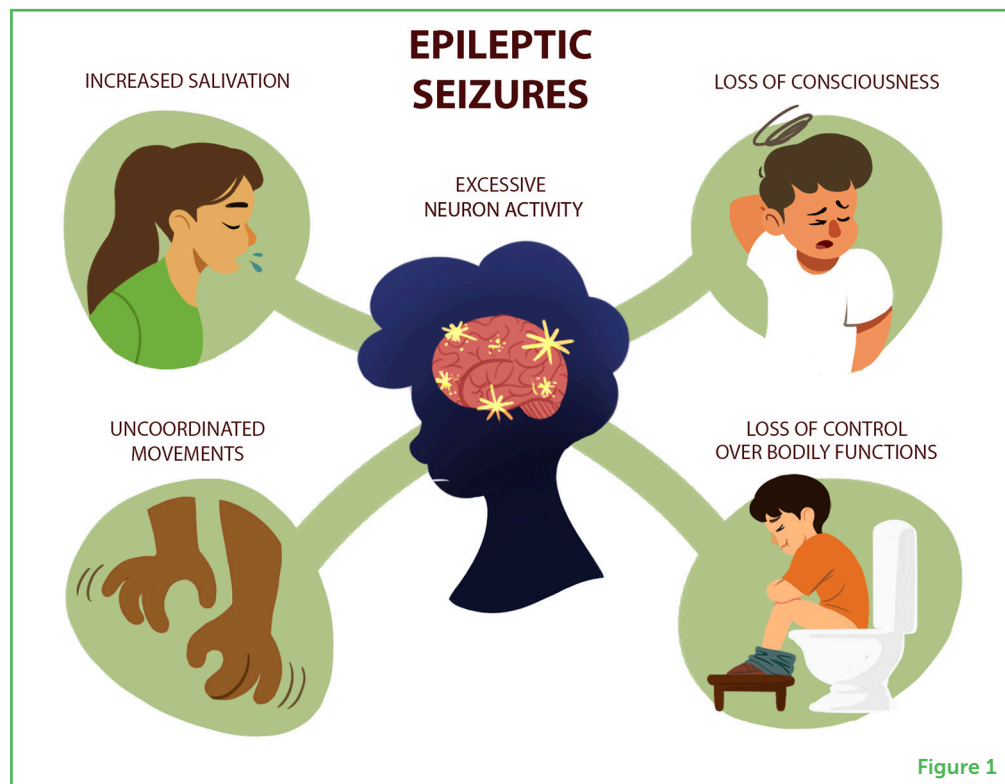


Figure 1

options are needed. Without effective treatment, epileptic people have reduced chances of living normal lives. Luckily, there are scientific studies seeking new treatment options!

## EFFECTS OF MARIJUANA COMPOUNDS

One of those studies uses substances from *Cannabis sativa*, a plant also known as marijuana, pot, or weed. You may be wondering how a plant used as a recreational drug could also be used to treat diseases! For centuries, plants were the only medicines available to people, and marijuana has been used for a long time to treat diseases, due to its effects on the brain. When marijuana is overused, however, a person might hear or see things that do not exist and might experience memory loss and other potentially dangerous side effects [3]. Scientists discovered that marijuana's many effects are due to multiple chemical components, called **cannabinoids**, that are contained by the plant. Among them, tetrahydrocannabinol (THC) and cannabidiol (CBD) are the most important ones [3].

THC is the cannabinoid that can alter a person's perception of the world, by changing brain function. People enjoy its effects, but overuse eventually results in difficulty with thinking, memory loss, mood swings, and negative effects. For this reason, marijuana is often considered a drug of abuse. In contrast, CBD does not cause negative effects in the brain. This cannabinoid has the most medicinal applications. It protects the brain, decreases depressive thoughts, and

### CANNABINOIDS

Natural or artificial compounds present in marijuana. Cannabinoids bind to the cannabinoid receptors CB<sub>1</sub> and CB<sub>2</sub>.

eases symptoms of other brain diseases, such as epilepsy [4]. But how does CBD work in the brain?

## DISCOVERY OF A NEW CHEMICAL SYSTEM IN THE BRAIN

By studying cannabinoids, scientists discovered a new chemical system in the brain, named the endocannabinoid system. The endocannabinoid system has three main parts. First, we have the **endocannabinoids** (eCBs), which are substances similar to cannabinoids but produced by the body. eCBs belong to the family of neurotransmitters, which pass information between neurons. eCBs bind to the second component of the eCB system, cannabinoid **receptors**. eCBs and their receptors work like a key and a lock—when the key is inserted into the lock, the “door opens” and a signal is transmitted from the outside of the cell to the inside. There are two types of cannabinoid receptors, called CB<sub>1</sub> and CB<sub>2</sub>. Certain enzymes are the third part of the system. Enzymes control the process—they produce and remove eCBs, ensuring that they are only present when needed.

Did you know that neurons produce many kinds of neurotransmitters? Tiny “bags” within the nerve cells, called **synaptic vesicles**, produce and store most neurotransmitters. Neurons communicate with each other by releasing these “bags.” Do you remember the comparison of neurons to teachers and students? Although they can all learn from each other, the teacher usually transmits more information to the student. In the brain, the “teacher” neurons (called presynaptic neurons) release neurotransmitters into the spaces between the two neurons, called the **synaptic cleft**. The information reaches “student” neurons (called postsynaptic neurons) and binds to the receptors on their surfaces (Figure 2). This signal transmits information from one cell to the other.

The endocannabinoid system is somewhat different! eCBs are produced only when we need them. They are not stored in synaptic vesicles and are released in the *opposite* direction, which is known as **retrograde neurotransmission**. This is like students transmitting information to teachers (Figure 3) [5]. Both eCBs and cannabinoids from marijuana act through the brain’s CB<sub>1</sub> and CB<sub>2</sub> receptors.

Cannabinoid receptors are found throughout the body. CB<sub>1</sub> is mostly found in the brain, where this receptor plays a role in attention, memory, emotions, learning, pleasure, appetite, mood, pain, and motor ability. CB<sub>2</sub> receptors help to control the immune system, which protects the body from disease-causing organisms [5]. Since there are cannabinoid receptors throughout the body, the endocannabinoid system participates in the development and proper functioning of many structures, including the brain. But in

### ENDOCANNABINOIDS

Neurotransmitters produced by our body, similar to cannabinoids, that helps regulate various body processes.

### RECEPTORS

Cellular structures that allow the interaction between the cell and specific molecules. This lock-and-key interaction can lead to the transmission of signals inside and outside the cells.

### SYNAPTIC VESICLE

Compartments that store various neurotransmitters that are released at the synapse.

### SYNAPTIC CLEFT

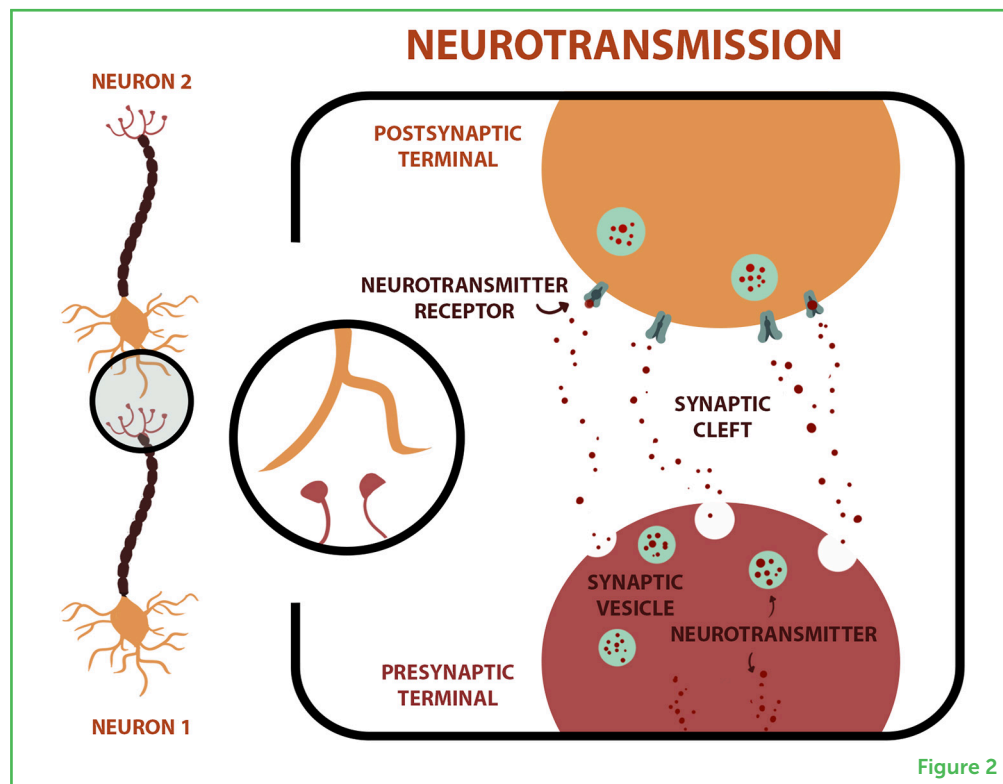
Small space between pre and post neurons where neurotransmitters are released to perform their function, binding to receptors and generating a physiological response.

### RETROGRADE NEURO-TRANSMISSION

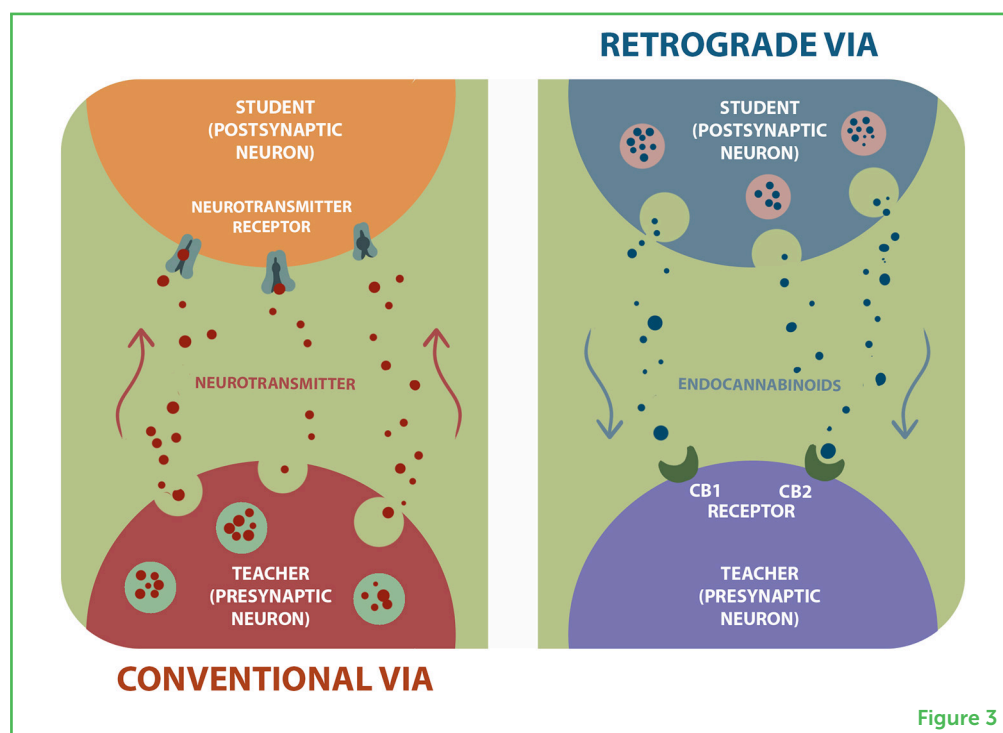
Process by which a neurotransmitter, such as endocannabinoids, is released by postsynaptic neurons and “travels backwards” to bind to receptors on the presynaptic neurons.

**Figure 2**

Neurons communicate with each other across a space called the synaptic cleft in which neuron 1 (pre-synaptic) communicates with neuron 2 (postsynaptic). In the close-up right image, synaptic vesicles inside the “teacher” (presynaptic) neuron release neurotransmitters into the synaptic cleft. These molecules bind to receptors on the “student” (postsynaptic) neuron.

**Figure 2****Figure 3**

On the left image, we show the conventional *via* in which “teacher” neuron (presynaptic) releases neurotransmitters. These neurotransmitters bind to “student” neuron (postsynaptic) receptors. On the right side, the image represents the retrograde *via*, in which neurotransmission happens backwards: endocannabinoids released from “student” neuron (postsynaptic) bind to receptors CB<sub>1</sub> and CB<sub>2</sub> on “teacher” neuron (presynaptic).

**Figure 3**

some diseases, like epilepsy, the endocannabinoid system does not work well [4]. Therefore, substances that regulate the function of the endocannabinoid system might be a promising way to treat diseases like epilepsy.

## USE OF CBD FOR EPILEPSY TREATMENT

Scientific studies suggest that CBD reduces seizures in different types of epilepsy that affect adults and children. In addition, CBD has fewer adverse effects when compared to other medications used to treat epilepsy. Although the results are promising, larger clinical studies are needed.

Scientists still do not fully understand how CBD works in the brain to help control epilepsy. One thing we know is that THC binds to cannabinoid receptors in the brain, which mediates its effects in that organ, but CBD does *not* bind to those receptors. Instead, CBD seems to act on other receptors and pathways in the brain to facilitate the functioning of the endocannabinoid system. CBD can stimulate the production and release of eCBs, which seems to inhibit the excessive activity of neurons that causes epileptic seizures [4]. Although CBD appears to be safe and has promising results in the treatment of epilepsy, further studies are needed to determine exactly how it works [1, 2]. Science is done that way—each research study is a piece of the puzzle and, the more pieces we have, the greater the chances that we can help people.

## CONCLUSION

The study of cannabis and the endocannabinoid system can provide important scientific discoveries. Separating CBD from other marijuana compounds and using it to treat epilepsy can be a great alternative for patients that suffer from this disease. When we talk about the efficacy and safety of CBD as a medicine, we are not saying that smoking marijuana is safe—it contains several compounds that might be bad for your health, including THC. Even CBD is not a miraculous compound! Like any other medicine, it may work well for some people but not for others. That is why only doctors can advise us about which medicines to take. This article is just one example of how science can make discoveries that can have positive impacts on our lives, including treatments for important diseases!

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## REFERENCES

1. Falco-Walter, J. J., Scheffer, I. E., and Fisher, R. S. 2018. The new definition and classification of seizures and epilepsy. *Epilepsy Res.* 139:73–9. doi: 10.1016/j.eplepsyres.2017.11.015
2. O'Connell, B. K., Gloss, D., and Devinsky, O. 2017. Cannabinoids in treatment-resistant epilepsy: a review. *Epilepsy Behav.* 70(Pt B):341–8. doi: 10.1016/j.yebeh.2016.11.012
3. Mechoulam, R., Hanuš, L. O., Pertwee, R., and Howlett, A. C. 2014. Early phytocannabinoid chemistry to endocannabinoids and beyond. *Nat. Rev. Neurosci.* 15:757–64. doi: 10.1038/nrn3811
4. Zuardi A. W. 2008. Cannabidiol: from an inactive cannabinoid to a drug with wide spectrum of action. *Revista Brasileira de Psiquiatria* 30:271–80. doi: 10.1590/s1516-44462008000300015
5. Lopes, J. B., Bastos, J. R., Costa, R. B., Aguiar, D. C., and Moreira, F. A. 2020. The roles of cannabinoid CB<sub>1</sub> and CB<sub>2</sub> receptors in cocaine-induced behavioral sensitization and conditioned place preference in mice. *Psychopharmacology.* 237:385–94. doi: 10.1007/s00213-019-05370-5

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## YOUNG REVIEWERS



### ANYA, AGE: 15

Hello! My name is Anya. I am interested in sciences, particularly neuroscience and psychology. I like writing as well and think that these two areas could be combined to have positive effects on the world.



### MARINA, AGE: 14

Hi, my name is Marina and I am 14 years old. I enjoy playing sports such as volleyball, touch football, basketball, soccer and rugby. My favorite subjects at school are science and math along with Health and Physical Education. In my spare time I enjoy to going to the beach and go shopping with friends.

## AUTHORS



### ALINE DE CASTRO SANTOS

I am a doctoral student in physiology and pharmacology at the University Federal of Minas Gerais-Brazil. My research is about the relationship between the endocannabinoid system and drug addiction, which includes studying how marijuana compounds work in the brain. I am also part of a scientific communication project to spread scientific information throughout the population, using simple language. Using my voice to communicate science to society is one of the best choices I have ever made!



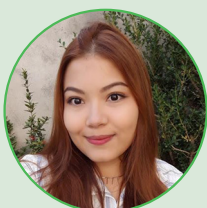
### ANA CLARA MATOSO MONTUORI DE ANDRADE

I am a postdoctoral student at University Federal of Minas Gerais-Brazil. I am a biologist with a master's degree and Ph.D. in biochemistry and immunology. I try to understand the influence of intestinal microbes on the immune system, to help us fight lung diseases. I have always been passionate about science and I hope that science will become increasingly accessible to everyone, and that everyone will understand its importance for themselves and for the world.



### ELIZA MATHIAS MELO

I am a biologist with a master's degree in biochemistry and immunology from University Federal of Minas Gerais-Brazil. For my master's degree, I worked with the pathogenic fungi *Paracoccidioides brasiliensis*. In my Ph.D. I worked evaluating anti-inflammatory drugs for pneumonias treatment. I have always enjoyed learning about the biology of microorganisms and infectious lung diseases, and sharing knowledge about therapeutic discoveries and how interesting science is.



### FLÁVIA RAYSSA BRAGA MARTINS

I am a biologist working on a master's degree in genetics at the University Federal of Minas Gerais-Brazil. My research aims to understand how chronic alcohol consumption affects bone marrow, and the consequences for the immune response in the lungs. I have always been a curious student, and this gave me a passion for science and made me want to work hard to understand a little bit more about living



things. I am part of a scientific dissemination project that allows me not only to learn but also to bring science to people who usually do not have contact with it.



### **ISABELLA LUISA DA SILVA GURGEL**

I am a Ph.D. student in the genetics program at the University Federal of Minas Gerais-Brazil. My research aims to understand the roles of genes from a fungus that can cause infections in people with weak immune systems. I am also part of the science communication project "Science for You," through which we spread scientific information across the population, using simple language. I believe that bringing science closer to society makes people understand the importance of our work for their lives. To be part of such a project is amazing!



### **ISABELLE CRUZ ZENOBIO**

I am studying pharmacy at the University Federal of Minas Gerais-Brazil. I do research about chronic alcohol consumption and its effects on the immune system. I am also part of the project "Science for You," in which we try to spread scientific knowledge using simple language. Science allows me to learn a little more and challenge myself every day. I am grateful to do what I love and for the lessons I exchange with my work partners.



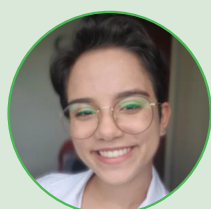
### **JORDANA PERUCHI FONTIS**

I am studying medicine at the University Federal of Minas Gerais-Brazil. I am performing clinical research about the quality of life of people living with liver diseases. I participate in a project that aims to spread and popularize scientific knowledge, called "Science for You." I understand that, as a graduate student at a Brazilian public university, sharing the knowledge I acquire in college is one of my duties as a citizen.



### **LUAN TAVARES DE SOUZA**

I study animation and digital arts at the University Federal of Minas Gerais-Brazil. I work with illustration, animation, and art-related stuff, but I have joined the CPV project "Science for You" because I think it is super important to create dialogue between the university and society, so both can learn from each other. I also believe that this project is a great way to spread science-related topics in an accessible way, like through social media, so it can reach multiple and varied groups of people.



### **MARIA LUIZA ROCHA GUIMARÃES**

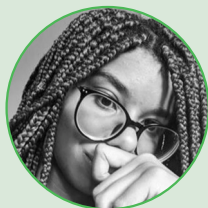
I am a University Federal of Minas Gerais undergraduate, majoring in pharmacy. I am part of "Science for You," a project dedicated to spread of scientific knowledge. I am also involved in an undergraduate research project in which we study a new treatment for Alzheimer's disease, using a plant called mangabeira. I have always been interested in science and all the possibilities it can offer. It is a big pleasure to be involved in scientific research and to share its results with other people.



### **NATHALIA LUISA SOUSA DE OLIVEIRA MALACCO**

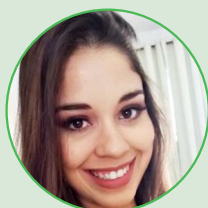
I am a postdoctoral fellow at the University Federal of Minas Gerais-Brazil. I have a bachelor's degree and I teach biology, but my work deals with genetics, immunology, and microbiology. My current project is to understand the role of molecules called chemokine receptors in infectious diseases. I have always been a good student, highly interested in learning and teaching, and constantly willing to expand my

knowledge. I also have a passion for spreading science knowledge, to communicate and explain to everyone why science is so important for our lives.



### **RENATA LUIZA QUINTINO PAULINO**

My name is Renata, I am 21 years old, and I am a pharmacy student at the University Federal of Minas Gerais-Brazil. I love books, movies and series, especially if they are romantic. I am still new to college but through the program “Science for You,” I have discovered a new way of seeing science. Science is closer than you think—when you turn on the television, cook with your parents, or set off fireworks. Science is in the little details of everyday life, and that is magical.



### **THAÍS SALVIANA RIBEIRO**

I have a bachelor’s degree in biomedical sciences and I have always loved science! Ever since I was little, I questioned how nature and our bodies worked, and this curious and passionate mind led me along the scientific path that I still follow. I recently got a master’s degree in pathology, the area of medicine responsible for studying and explaining how diseases affect our bodies, and my research focused on melanoma, an aggressive skin cancer. I currently work with molecular diagnosis of COVID-19, and I help to spread science on social media. My hobbies are reading, cooking, and playing the ukulele.



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