

**IMPACT** Health Media PRESENTS

# THE HEALING POWER OF THE ENDOCANNABINOID SYSTEM

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## NATURE'S SOLUTION FOR:

- stress/anxiety
- depression
- insomnia
- fatigue
- pain/inflammation
- digestive issues
- brain function
- and more!

\$4.95



# Influencing the Endocannabinoid System (ECS)

With non-cannabis, plant-based herbals and botanical phytocannabinoids

**CB<sub>1</sub>**

**MAIN CANNABINOID RECEPTORS**

UNLOCKING THE HEALTH POTENTIAL OF THE ECS

**CB<sub>2</sub>**

## PHYTOCANNABINOIDS

🔑 GINGER 🔑 ECHINACEA 🔑 MAGNOLIA

Interact with endocannabinoid receptors

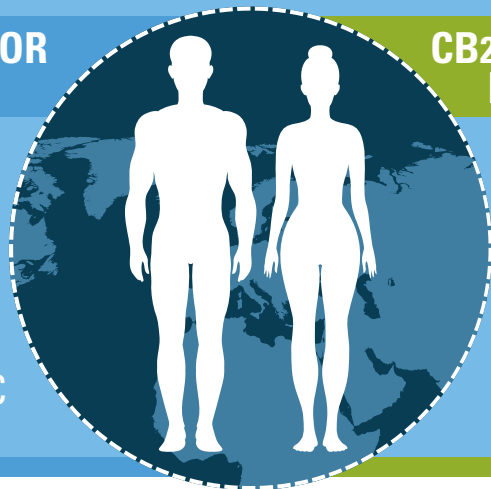
Are not derived from cannabis

Do not contain THC



### CB<sub>1</sub> RECEPTOR LOCATIONS

BRAIN  
CENTRAL NERVOUS SYSTEM  
NERVES  
CB<sub>1</sub> SPECIFIC ORGANS



### CB<sub>2</sub> RECEPTOR LOCATIONS

CB<sub>2</sub> SPECIFIC ORGANS  
IMMUNE SYSTEM CELLS

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## A REMARKABLE DISCOVERY

### 600-million-year-old healing system revealed

THE HUMAN BODY and mind are beautifully complex and rely on the interrelationship of various systems working in harmony and balance. While the processes behind many of the body's systems have been understood for quite some time, it was not until 1988 that a researcher uncovered a 600-million-year-old system that is now regarded as the most important physiological process for establishing and maintaining human health.

This system, called the endocannabinoid system (ECS), is named after the cannabis plant that led to its discovery. It is now known that the ECS is critical to regulating the proper function of a wide range of body processes. Specifically, the ECS plays an important role

#### THE ECS IS CRITICAL TO REGULATING THE PROPER FUNCTION OF A WIDE RANGE OF BODY PROCESSES

in your nervous system, immune system, digestive system, endocrine glands, brain, heart, lungs, kidneys, liver, spleen, bones, muscles, blood vessels and cells, lymph cells, and fat cells.

But while the discovery of the ECS was due to the cannabis plant, this system has little to do with the psychoactive component of marijuana, tetrahydrocannabinol (THC), and more to do with compounds that your body makes as well as factors in food and medicinal plants. In fact, the ECS occurred in nature before cannabis did, and thus can be influenced by many more factors than just marijuana—including your diet and lifestyle choices.

The purpose of the ECS is to serve as a master conductor, sending chemical messages and triggering biological actions throughout the body that are critical to health and well-being. The outcome of this delicate balancing act is to create homeostasis—that internal drive within every cell in your body and

# THE ENDOCANNABINOID SYSTEM REGULATES

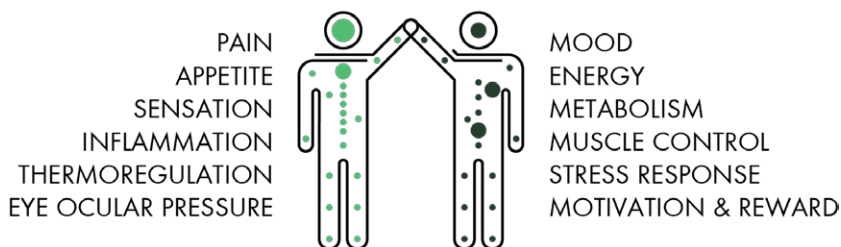


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brain to maintain balance and promote health within its internal environment, even when faced with external changes.

The ECS regulates many key aspects of your physical, emotional, and mental health, including:

- Appetite, digestion, and hunger
- Cellular energy
- Emotions
- Memory
- Metabolism
- Mood
- Motivation, pleasure, and reward
- Motor control
- Immune function
- Inflammation
- Pain
- Reproduction and fertility
- Sleep
- Stress response
- Temperature regulation

In the following pages, you'll find a comprehensive look at how the ECS works; how marijuana affects the ECS; and how factors like diet, dietary supplements, stress, and your lifestyle choices can have a profound impact on this vitally important system—and, ultimately, your overall health.

# What we know and how we learned it

IN 1964, ISRAELI RESEARCHER Dr. Raphael Mechoulam identified THC as the main active ingredient in cannabis. Three decades later, he began studying exactly how THC works in the body and brain. That led to his discovery of a complex and elegant cell-signaling system triggered by not only THC, but other compounds as well.

Dr. Mechoulam named this system endocannabinoid because “endo” means within the body and “cannabinoid” highlights the role the cannabis plant played in the discovery.

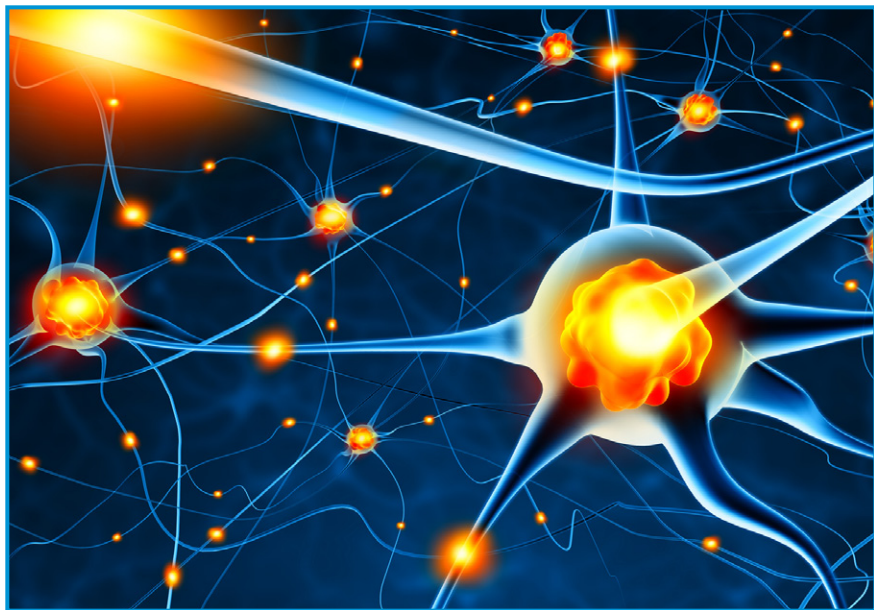
To put the magnitude of this discovery into perspective, an ECS exists in all mammals, birds, reptiles, and other invertebrates. And despite the relative infancy of the monumental discovery of the ECS, there have been over 20,000 studies published in the last 20 years containing the word “cannabinoid.”

## The biological nuts and bolts of the ECS

The ECS is presently known to include:

- Receptor sites on cells called CB1 and CB2
- Compounds known as endocannabinoids produced in the body from dietary fats like anandamide that bind to CB1 and CB2 receptors
- Enzymes that impact the manufacture and metabolism of these endocannabinoids

Receptors send vital information to cells, organs, and the nervous system, and are critical to maintaining optimal health and homeostasis. In the human body, the ECS is believed to have more cellular receptor sites than any other receptor system.



Molecules circulate throughout the body and then bind to the cell's receptor to stimulate action. In the human body, the ECS is believed to have more cellular receptor sites than any other receptor system.

Basically, receptors on cell surfaces are similar to locks on a door. When the right “key,” in the form of a chemical molecule, binds to the cellular receptor, it relays a specific message to the cell that helps it do its job. Most hormones work in this manner. For example, when insulin binds to its receptor on a cell, it causes that cell to ultimately allow blood sugar (glucose) to enter the cell.

The two primary cell cannabinoid receptors, CB1 and CB2, are found throughout the body. However, they tend to concentrate in certain areas. For example, CB1 receptors are abundant

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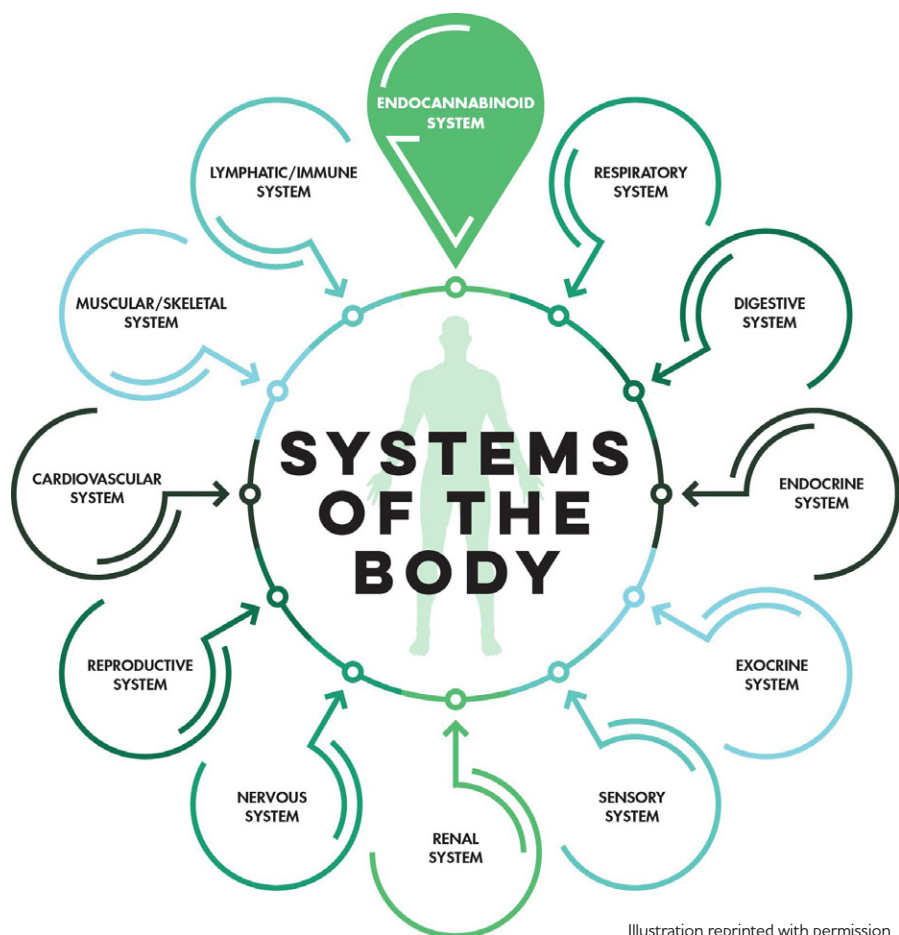


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in the brain, while CB2 receptors are more often found on immune cells, in the gastrointestinal tract, and in the peripheral nervous system.

The widespread distribution of cannabinoid receptors shows just how important the ECS is to overall bodily function and health. In fact, activation of CB1 and CB2 receptors changes cellular function, including gene expression and electrical excitability of cell membranes. It is a very powerful event.

## Endocannabinoid deficiency syndrome

Considering how important the ECS is to your body and brain, it's not a surprise that a lack of endocannabinoid activity is thought to be linked to debilitating ailments such as fibromyalgia, migraine, multiple sclerosis, seizure disorders, chronic fatigue, irritable bowel syndrome, and more.

In 2003, Dr. Ethan Russo developed a term for this condition: clinical endocannabinoid deficiency syndrome (CEDS). Since then, there's been an even greater appreciation for the role of the ECS in not only the ailments listed above, but others as well.

## The bliss molecules

After he identified THC, Dr. Mechoulam and his fellow researchers in Israel shifted their focus to finding the natural compound produced in the body

**Clinical endocannabinoid deficiency syndrome (CEDS) = reduced endocannabinoid activity that has been linked to a variety of illnesses**

Whether CEDS is the result of poor diet, lack of exercise, drug abuse, environmental toxins, or genetic factors, endocannabinoid deficits are associated with a reduced ability or inability to adapt to chronic stress. Prolonged exposure to stress depletes endocannabinoid tone, and this, in turn, has an adverse impact on a plethora of physiological processes.

So how do you guard against CEDS? By boosting the ECS. And scientific evidence indicates that the best way to do this may be by focusing on non-cannabis approaches such as diet, dietary supplements, and healthy lifestyle choices.

But before we discuss how to optimize the ECS through these non-cannabis approaches, we need to provide a more complete overview of the ECS. This will allow you to see the magic of how a wide range of plant compounds and dietary factors work harmoniously to maximize this beautiful system.

that binds to cannabinoid receptors. Finally, after more than two decades of searching, they discovered the compound: a type of essential fatty acid called anandamide. Dr. Mechoulam and his colleagues chose this name because its root comes from the Sanskrit word *ananda*, which means bliss.

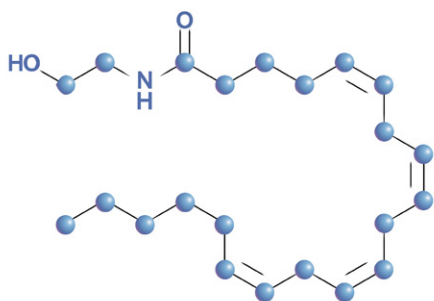
When anandamide binds to the cannabinoid receptor in the emotion center in the brain, it produces a mild state

of bliss, as well as a calming effect. But that's not all it does. Research shows it's important for memory, motivation, higher thought processes, and movement control. It also plays an important role in appetite control and the perception of pain.

In 1995, three years after they identified anandamide, Dr. Mechoulam's group discovered a second endocannabinoid—a fatty-acid metabolite with a less elegant name: 2-arachidonoylglycerol (2-AG). It is a little different than anandamide because it's able to bind to both CB1 and CB2 receptors.

Both anandamide and 2-AG are now known to play a main role in direct cell-to-cell communication. In essence, these endocannabinoids make sure all of the cells of a particular type, or in a specific area of the body or brain, are rowing at the right pace and in the right direction.

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**ANANDAMIDE**

## MEDICAL MARIJUANA

### When it comes to the ECS, all cannabinoids aren't created equal

WHILE THC GETS THE MOST ATTENTION, there are a total of 150 cannabinoids unique to cannabis. In addition, the plant contains a lot of other active compounds. Dr. Mechoulam, along with top cannabis researchers, is convinced that all of the components of cannabis work together to produce what is called the “entourage effect.” There is growing scientific support of this entourage effect. And, it is not just related to compounds found in cannabis, but also other compounds found in a variety of different foods, herbs, spices, and natural products.

This became apparent when the synthetic version of THC, the drug Marinol, hit the market. People found Marinol wasn't as effective as using the whole marijuana plant. This led to research on the cooperative interactions of the other cannabinoids, as well as the various other active compounds in cannabis.

And that, in turn, spurred research into the effect of various cannabinoids on the ECS.

### Does THC make your ECS “high”?

When a person smokes or ingests marijuana, THC quickly overwhelms the ECS by attaching to CB1 receptors throughout the brain and body. This is basically a distorted and significantly amplified version of what anandamide does. THC so overpowers the endocannabinoid system that it basically wipes out the ability of anandamide to fine-tune communication between brain cells.

While it is easy to focus on the psychoactive effects of THC, it's important to remember that because cannabinoid receptors are in so many parts of

the brain and body, THC affects virtually every cell you have. For instance, marijuana can impair certain mental functions like reaction time, memory, and judgment by actually changing how the ESC works in certain brain areas. It can also affect the parts of the brain that make us feel good, or “high.”

Marijuana also produces some short-term physical effects, including reddening of the eyes, a reduction in intraocular pressure (hence its use in glaucoma), dry mouth, muscle relaxation, and a sensation of cold or hot hands and feet.

There is currently a great deal of excitement about the medical use of marijuana, based on its THC content as well as other cannabinoids such as cannabidiol (CBD). However, while there is strong scientific evidence for marijuana’s effects on glaucoma, nausea and vomiting associated with chemotherapy, loss of appetite and weight loss in HIV/AIDS, chronic pain, and

spasticity due to multiple sclerosis or spinal cord injury, there is not much data for many other indications, such as epilepsy, insomnia, and depression. That is all changing rapidly, however, as there is intense new interest in expanding the uses of medical marijuana.

In regards to relieving pain, THC doesn’t act like opioid drugs such as oxycodone and morphine. Instead, it reduces the perception of pain. Also, can-

nabis and pain-relieving drugs are co-agonists, meaning that one magnifies the effect of the other—cannabis enhances the pain-relieving effects of opioids and vice versa.

This is key for people in severe pain, because it allows them to take lower, but still-effective dosages of both marijuana and opioids. Additionally, CB1 receptors are not present in the part of the brain that regulates heart rate and respiration, so unlike with narcotics, there is no lethal dose for THC.

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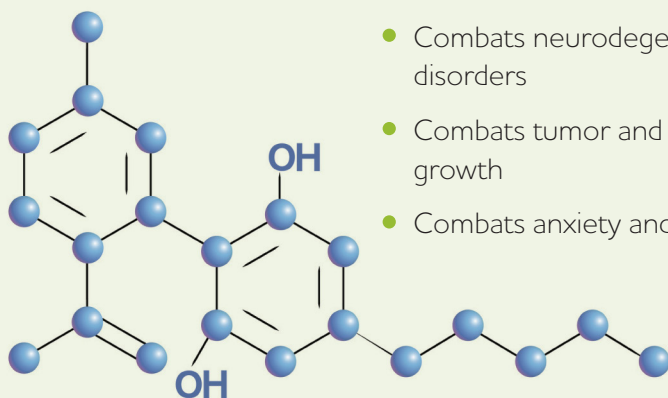
## A closer look at CBD

CBD is a non-psychoactive cannabinoid found in marijuana that impacts the entire ECS. Consequently, it's showing tremendous promise for improving overall health.

Since CBD does not bind to CB1 receptors in the same manner as THC, it doesn't make people feel high. In fact, CBD reduces the euphoria produced by THC.

Currently, there is great focus on THC+CBD combinations for a number of different health conditions, including epilepsy, anxiety, insomnia, depression, schizophrenia, multiple sclerosis, and inflammatory disorders. Unfortunately, most of this evidence comes from animals, since very few CBD studies have been carried out in humans. And the studies that have been done on CBD alone, without THC, have not shown much of an effect, except for specific and fortunately rare forms of epilepsy.

## POTENTIAL APPLICATIONS OF CBD



CANNABIDIOL

- Reduces nausea and vomiting
- Suppresses seizure activity
- Combats psychiatric disorders
- Combats inflammatory disorders
- Combats neurodegenerative disorders
- Combats tumor and cancer cell growth
- Combats anxiety and depression

Perhaps you saw the 2013 CNN documentary “Weed.” This show created quite a rush to Colorado to get Charlotte’s Web, a high-CBD, low-THC cannabis extract marketed as medical cannabis under state laws.

The extract was named after Charlotte Figi, who was born in 2006 and suffers from a genetic disorder (Dravet syndrome) characterized by multiple, repeated epileptic seizures. At age 5, after her first dose of medical marijuana, Charlotte had a dramatic reduction in seizures.

There are now several different forms of CBD on the market, including oil that’s taken orally, capsules, topical creams and balms, and vape liquid that’s used in refillable vape devices.

Additionally, in 2018 the drug company GW Pharmaceuticals is planning to debut Epidiolex, a drug with CBD as its active ingredient, for the

treatment of Dravet syndrome. GW Pharmaceuticals also markets Sativex, a specific combination of extracts from cannabis that provides an equal ratio of THC to CBD. Sativex has been approved in several countries, including Canada (2005) and the United Kingdom (2010), as a mouth spray to alleviate pain, spasticity, overactive bladder, and other symptoms of multiple sclerosis.

Internet marketers and others have jumped on the CBD bandwagon and are hyping it as a virtual cure-all. However, there are a couple important considerations for consumers, aside from legal matters: Does CBD oil produce benefits and if so, at what dosage?

To answer the first part of the question, yes there is some evidence that products that contain only CBD can produce some benefits. But the results were not that impressive in double-blind, placebo-controlled clinical trials, even with high dosages of CBD (400–1,200 mg a day). For example, several studies found that 400–600 mg of CBD per day was actually less effective at treating anxiety than a placebo.

The closest thing to a positive study with a CBD-only product was done in people with insomnia. A dosage of 160 mg per day was shown to be more effective than a placebo for sleep duration and dream recall. Lower dosages of 40–80 mg per day showed no benefit over the placebo on sleep duration or on the time required to go to sleep.

One of the reasons why animal and in vitro (test tube) studies show great effects with CBD, while human studies often show the opposite, may be due to the poor absorption of CBD when taken orally. While studies show that vaporized CBD can have about 40 percent bioavailability, only about 6 percent of the oil is absorbed in humans.

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# INTERNAL NOURISHMENT

## The best dietary ways to support your ECS

RESEARCH INTO HOW DIET AND LIFESTYLE impact the ECS is only in the very early stages. However, what is known is that steps can be taken to:

- ① Support the body's natural production of endocannabinoids
- ② Harness natural products to modulate the breakdown of endocannabinoids like anandamide and prolong their effectiveness in the body
- ③ Utilize non-cannabis-derived, plant-based compounds to activate CB1 and CB2 receptor sites

### Focus on fats

Eating a diet rich in “good” fats is critical for the proper functioning of the ECS. Simply stated, without the right type of fats in their membranes, cells do not function properly—and neither will the ECS.

Omega-6 fatty acids, longer-chain saturated fat, and trans fats are all considered “bad” fats, and are linked to many diseases—especially when you also don't eat enough “good” monounsaturated fats, medium-chain saturated fat, and omega-3 fatty acids. Not surprisingly, this same dietary pattern is also associated with impaired function of the ECS.

Foods that contain omega-3 fatty acids are critical because they are considered “essential fatty acids.” This term refers to fatty acids that are required for key biological processes in the body; however, these fats cannot be manufactured in the body so they must come from the diet. On page 18 there is a list of these “good” fats that should be eaten on a regular basis, as well as a list of “bad” fats that should be avoided whenever possible.



The following table lists specific sources of each type of fat.

| GOOD FATS  | BAD FATS  |
|--|---|
| Monounsaturated fats<br>Nuts and seeds<br>Olive, avocado, canola, and macadamia-nut oils<br>Sunflower oil (high oleic only)  | Trans fats<br>Partially hydrogenated vegetable oil<br>Shortening<br>Margarine<br>Many baked goods and crackers (look for “trans fats” on the label)   |
| Alpha-linolenic acid, an omega-3 fatty acid<br>Flaxseeds and flaxseed oil<br>Walnuts<br>Chia seeds<br>Canola oil<br>Hemp seed oil (considered the best source of fatty acids in terms of omega-3 to omega-6 ratio) | Linoleic acid, an omega-6 fatty acid<br>Most vegetable oils, including corn, grapeseed, safflower, soy, and sunflower                                 |
| EPA and DHA omega-3 fatty acids<br>Coldwater fish such as salmon, mackerel, herring, trout, tuna, and sardines<br>Fish-oil supplements   | Oxidized fats<br>Fried foods<br>Charbroiled meat  |
| Medium-chain saturated fats<br>Coconut oil<br>Grass-fed meat and dairy<br>Organic, free-range chicken and eggs<br>Wild salmon  | Longer-chain saturated fats<br>High-fat meat and dairy<br>Grain- or soy-fed meat and dairy<br>Conventionally raised chicken and eggs<br>Farmed salmon |

Although the anandamide fat that is key to ECS function is derived from arachidonic acid, an omega-6 fatty acid found in meat and dairy, studies indicate that too much arachidonic acid in the diet is not only associated with greater inflammation in the body, but also does not lead to increased levels of endocannabinoids in the brain—a key target area of the ECS.

On the flip side, there are two types of fat that do increase brain and body levels of endocannabinoids, as well as enhance endocannabinoid receptor binding: monounsaturated fats (particularly olive oil) and eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) omega-3s from fish oils.

Interestingly, both EPA and DHA are converted to compounds that have been recently shown to have affinity to CB1 and CB2 endocannabinoid receptors. So it's not surprising that data indicates that a deficiency of omega-3 fatty acids is particularly harmful to the ECS.

But unfortunately, while most Americans eat way too many omega-6s, they suffer a relative deficiency of omega-3s. The result is not only a poorly functioning ECS, but also an increased risk for heart disease and about 60 other conditions, including cancer, arthritis, stroke, high blood pressure, skin diseases, and diabetes.

To boost your omega-3 levels, take a high-quality fish-oil supplement that provides at least 1,000 mg of EPA and DHA daily. For therapeutic purposes, such as reducing inflammation or lowering triglyceride levels, you can boost that dosage to 3,000 mg of EPA and DHA per day.

The best way to increase your monounsaturated fat intake is to follow a Mediterranean diet. This diet is good for the ECS in other ways as well.

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## What is the Mediterranean diet?

The Mediterranean diet refers to eating patterns typical of southern European regions like Greece and Italy.

For many reasons, olive oil gets a lot of credit for the health benefits of the traditional Mediterranean diet. But research clearly shows there is a significant synergy among all of the components of the diet, rather than one specific factor being responsible for the multiple health benefits.

In addition to supporting a balanced ECS, this diet has numerous health benefits that have been confirmed by scientific research. It's perhaps one of the most widely studied diets in the scientific literature. The Mediterranean diet has been shown to support health in a variety of ways including:

- Reduced risk of heart disease
- Reduced risk of many forms of cancer
- Supports brain function and healthy cognition
- Enhances bone health
- Improves mental health by contributing to reduced depression and anxiety

The chief tenets of the Mediterranean diet include:

- Extra-virgin olive oil as the principal source of fat
- Frequent consumption of seasonal, locally grown fruit, vegetables, beans, nuts, and seeds
- Minimally processed foods
- Low consumption (a few times a week at most) of sweets containing concentrated sugars or honey
- Low to moderate consumption (one to four times a week) of dairy products, principally cheese and yogurt
- Frequent consumption of seafood
- Low to moderate consumption of red meat, poultry, and eggs
- Moderate consumption of pasta, bread, and grains
- Low to moderate consumption of wine

# LIFESTYLE ADJUSTMENTS

## Stress-reduction techniques and dietary supplements can jump-start your ECS

ONE OF THE GREAT ENEMIES to the integrity and function of the ECS is stress. Job pressures, family arguments, financial pressures, time management, and even traffic are just a few of the “stressors” we are faced with on a daily basis. Whether acute or chronic, stress short circuits the incredibly complex ECS—making it vitally important to effectively deal with your stress triggers.

Of course, whether you are aware of it or not, you have developed a pattern for coping with stress. But unfortunately, most people rely on methods that ultimately do not support good health, such as overeating, uncontrolled emotional outbursts, feelings of helplessness, having a cocktail or beer, or smoking a cigarette.

It is important for you to identify any negative coping patterns and replace them with positive, effective stress-management methods. This involves four equally important areas:

- 1 Learning and using techniques to calm the mind and promote a positive mental attitude
- 2 Following a healthy lifestyle, including regular physical exercise
- 3 Eating a healthful diet
- 4 Utilizing key dietary and botanical supplements that support the ECS and reduce your body’s stress response



## Natural products to modulate the ECS

There are a number of plant extracts that support the ECS on multiple levels. Our top six include:

- **Clove oil (concentrated for  $\beta$ -caryophyllene).**

The pain-relieving aspects of clove oil are well known—mothers have used it to soothe the irritated gums of teething infants for generations. Clove oil contains several analgesic ingredients, but the one most researched for its effects on the ECS is  $\beta$ -caryophyllene. This compound is able to bind with great affinity to CB2 receptors, and is thought to be one of the ECS' primary mechanisms to reduce pain.



- **Echinacea purpurea.** Compounds in echinacea called alkylamides bind to CB2 receptors with great affinity, helping to boost the immune system. They also prolong the effects of anandamide on the ECS. Clinical studies on an alkylamide-rich extract have shown positive effects for relieving stress and anxiety.



- **Zanthoxylum or Sichuan pepper.** This tingly pepper contains alkylamides that display very strong affinity to CB1 and CB2 receptors. These compounds also influence transient receptor potential channels, which are involved in the electrical control of cells, help cells communicate with each other, and work closely with the ECS.



- **Peony.** This exotic flowering plant contains paeoniflorin, which has a number of benefits for endocannabinoid influence on cellular function. Like the alkylamides in Sichuan peppers, paeoniflorin influences transient receptor potential channels that are involved in the electrical control of cells and feelings of pain.



- **Ginger.** This herb has a multitude of health benefits. In particular, it helps the ECS mediate some pain, inflammation, and gastrointestinal effects. Ginger's volatile components also influence transient receptor potential channels.



- **Magnolia.** This fragrant, flowering tree contains magnolol, which is very effective at binding to both CB1 and CB2 receptors. Magnolia extracts also promote a relaxed mental state, which can significantly reduce anxiety.



## Exercise and The ECS

We've all heard about the "runner's high" when endorphins and other powerful feel-good chemicals are released from the brain when we exercise. As it turns out, the ECS is strongly linked to that runner's high. Researchers have found that exercise increases the sensitivity of cannabinoid receptors in the part of the brain that activates pleasure. When we exercise, we enhance the ECS. In a way, the ECS is designed to reward exercisers. The more we exercise the more the ECS is stimulated to pump out those positive hormones, which creates an incredibly important health-promoting cycle. Exercise has such a wide variety of health benefits that it's no surprise that it also helps enhance the ECS as well.



## PLANT PARTNERS

### Key natural products work in synergy with the ECS

BECAUSE THE ECS PLAYS SUCH A CENTRAL ROLE in promoting health, it makes sense to support its effects even further by taking certain dietary supplements. The following nutrients have synergistic effects with the ECS in key categories.

#### Pain and inflammation

- **Curcumin.** This yellow pigment of turmeric (*Curcuma longa*)—the chief ingredient in curry—is one of the most intensely researched natural products available today. A variety of clinical studies show that curcumin has anti-inflammatory activity. In addition, research shows that curcumin helps convert the plant-based omega-3 fatty acid ALA into the EPA and DHA omega-3s most commonly found in fish oil, which could be why vegans in India who eat a diet rich in curry have excellent levels of EPA and DHA, while vegans in North America do not.

For best results, use Theracurmin, an all-natural preparation that utilizes advanced techniques to reduce the particle size of curcumin, as well as dramatically increase its solubility. This significantly boosts the amount of



curcumin that can be absorbed by the body. Clinical studies have shown that Theracurmin can reduce tissue damage caused by inflammation; improve liver, heart, and joint function; and boost the quality of life for cancer patients.

- **Boswellia serrata.** This herb contains anti-inflammatory compounds—boswellic acids and triterpenoids—that complement the effects of curcumin. Since these compounds tend to be poorly absorbed in the body, we recommend the Casperome brand of boswellia. Casperome uses a technology called Phytosome to bind boswellia compounds with phosphatidylcholine (a key component of lecithin), which greatly enhance absorption.

## Cognitive enhancement and protection

- **Huperzine A.** This alkaloid isolated from the moss *Huperzia serrata* has been shown in clinical trials to block the breakdown of the neurotransmitter acetylcholine. This is key because low levels of acetylcholine are one of the main hallmarks of Alzheimer's disease.

Huperzine A has also been shown to be significantly more selective and substantially less toxic than the acetylcholine esterase (ACE) inhibitors currently used in conventional medicine to treat high blood pressure and Alzheimer's. In fact, Huperzine A has been available as a prescription drug in China since the early 1990s, and has reportedly been used by more than 300,000 people with no serious adverse effects.

- **Bacopa monnieri.** This herb has been used for centuries in Ayurvedic medicine, either alone or in combination with other herbs, as a memory and learning enhancer. Modern clinical trials have upheld this longtime use. In one of the first trials, 46 healthy volunteers, ages 18 to 60, had significant improvement in tests of their learning ability after as little as five weeks of taking 300 mg of bacopa extract daily. Another three-month study in 76 healthy adults, 40 to 65 years old, showed that bacopa helped improve memory.

## Stress and anxiety

- **Ashwagandha.** This herb is used in Ayurvedic medicine to help restore balance to the body and normalize body functions. Specifically, ashwagandha helps increase the body's resistance to stress and fatigue, and promotes mental clarity and concentration.
- **GABA (gamma-aminobutyric acid).** Research shows that low levels of this naturally occurring, major neurotransmitter can lead to several psychiatric and neurological disorders—primarily anxiety, depression, insomnia, and epilepsy.



PHOTO BY ROGER CULOS

We recommend a form of GABA called PharmaGABA, which is manufactured via a fermentation process that utilizes the probiotic *Lactobacillus hilgardii*. This natural GABA has been shown to produce relaxation effects not achieved by the synthetic form of GABA, which is produced from an industrial solvent.

Research suggests that PharmaGABA is easily absorbed and binds to GABA receptors outside the brain that ultimately lead to activation of the parasympathetic nervous system. As a result, within five to 30 minutes after digestion, PharmaGABA can produce what is referred to as the “relaxation response”—a physiological process that is in direct contrast to the stress or “fight or flight” response.

Specifically, research shows that PharmaGABA can promote relaxation by increasing the alpha to beta brainwave ratio, preserving salivary antibody production during stressful events, reducing cortisol and other markers of stress, decreasing the amount of time required to go to sleep, and increasing the time spent in deep-sleep stages and REM sleep.

## Depression

- **Saffron.** There is excellent data showing that saffron extract is not only a safe treatment for mild to moderate depression, but actually is as effective as Prozac.

In one study, 40 people with mild depression had a significant reduction in their depression after taking 30 mg a day of saffron extract for six weeks. In another study, 40 people with mild to moderate depression took either 15 mg of saffron extract, or 10 mg of Prozac, twice daily. After eight weeks, the saffron extract was found to be as effective for reducing depression as Prozac, with fewer side effects. In fact, while selective serotonin reuptake inhibitor antidepressants like Prozac can lead to significant weight gain, saffron extract actually promotes satiety and weight loss.



## Sleep

- **Passionflower (*Passiflora incarnata*).** Passionflower extract has been shown in studies to be helpful for relieving general anxiety and improving sleep quality.

In one study, 41 people drank either passionflower tea or a placebo tea every night for a week before going to sleep. The people who drank the passionflower tea reported a significantly better sleep quality than those drinking the placebo tea. In another study, a combination of herbs that included passionflower extract was found to be a safe and effective alternative to the insomnia drug zolpidem (Ambien).



## Are you doing all you can to support your ECS?

ONE OF THE MAJOR concepts in natural medicine is the power of synergy. Simply put, synergy is how different factors work together to achieve a positive effect greater than the sum of each individual factor. So in essence, synergy means that  $1+1+1$  does not equal 3, but something much, much greater.

That is certainly the case with the ECS. The ability of the ECS to promote homeostasis—that internal drive within every cell that leads to healing and ideal function—can be greatly enhanced by the clinically proven power of dietary supplements, along with good diet and lifestyle choices.

This is an exciting time for anyone interested in optimum health. Cutting-edge research is pointing to new directions in impacting health through enhancing the ECS. Hopefully, you are motivated to do all you can to support your ECS through diet, lifestyle choices, and dietary supplements.



## SELECTED REFERENCES

- Cani PD, Plovier H, Van Hul M, et al. Endocannabinoids—at the crossroads between the gut microbiota and host metabolism. *Nat Rev Endocrinol*. 2016 Mar;12(3):133–43.
- Fidyk K, Strzdała L, Szumny A.  $\beta$ -caryophyllene and  $\beta$ -caryophyllene oxide—natural compounds of anticancer and analgesic properties. *Cancer Med*. 2016;5(10):3007–3017.
- Gertsch J. Cannabimimetic phytochemicals in the diet—an evolutionary link to food selection and metabolic stress adaptation? *Br J Pharmacol*. 2016. doi: 10.1111/bph.13676. [Epub ahead of print].
- Hanuš LO, Meyer SM, Muñoz E, Taglialatela-Scafati O, Appendino G. Phytocannabinoids: a unified critical inventory. *Nat Prod Rep*. 2016 Nov 23;33(12):1357–1392
- Iannotti FA, Di Marzo V, Petrosino S. Endocannabinoids and endocannabinoid-related mediators: Targets, metabolism and role in neurological disorders. *Prog Lipid Res*. 2016;62:107–28.
- Katchan V, David P, Shoenfeld Y. Cannabinoids and autoimmune diseases: A systematic review. *Autoimmun Rev*. 2016;15(6):513–28.
- Kaur R, Ambwani SR, Singh S. Endocannabinoid System: A Multi-Facet Therapeutic Target. *Curr Clin Pharmacol*. 2016;11(2):110–7.
- Kendall DA, Yudowski GA. Cannabinoid Receptors in the Central Nervous System: Their Signaling and Roles in Disease. *Front Cell Neurosci*. 2017;10:294.
- Kim J, Li Y, Watkins BA. Fat to treat fat: emerging relationship between dietary PUFA, endocannabinoids, and obesity. *Prostaglandins Other Lipid Mediat*. 2013;104–105:32–41.
- McPartland JM, Guy GW, Di Marzo V. Care and feeding of the endocannabinoid system: a systematic review of potential clinical interventions that upregulate the endocannabinoid system. *PLoS One*. 2014;9(3):e89566.
- Morales P, Hurst DP, Reggio PH. Molecular Targets of the Phytocannabinoids: A Complex Picture. *Prog Chem Org Nat Prod*. 2017;103:103–131.
- Pertwee RG. Endocannabinoids and Their Pharmacological Actions. *Handb Exp Pharmacol*. 2015;231:1–37.
- Prospéro-García O, Amancio-Belmont O, Becerril Meléndez AL, Ruiz-Contreras AE, Méndez-Díaz M. Endocannabinoids and sleep. *Neurosci Biobehav Rev*. 2016;71:671–679.
- Proto MC, Fiore D, Laezza C, Bifulco M. Cannabidiol: State of the art and new challenges for therapeutic applications. *Pharmacol Ther*. 2017;S0163-7258
- Raichlen DA, Foster AD, Gardeman GL, et al. Wired to run: exercise-induced endocannabinoid signaling in humans and cursorial mammals with implications for the ‘runner’s high’. *J Exp Biol*. 2012;215(Pt8):1331–6.
- Russo EB. Beyond Cannabis: Plants and the Endocannabinoid System. *Trends Pharmacol Sci*. 2016 Jul;37(7):594–605.
- Sharkey KA, Wiley JW. The Role of the Endocannabinoid System in the Brain-Gut Axis. *Gastroenterology*. 2016;151(2):252–66.
- Smith SC, Wagner MS. Clinical endocannabinoid deficiency (CECD) revisited: can this concept explain the therapeutic benefits of cannabis in migraine, fibromyalgia, irritable bowel syndrome and other treatment-resistant conditions? *Neuro Endocrinol Lett*. 2014;35(3):198–201.
- Turcotte C, Blanchet MR, Laviolette M, Flaman N. The CB2 receptor and its role as a regulator of inflammation. *Cell Mol Life Sci*. 2016 Dec;73(23):4449–4470.
- Witkamp R, Meijerink J. The endocannabinoid system: an emerging key player in inflammation. *Curr Opin Clin Nutr Metab Care*. 2014;17(2):130–8.

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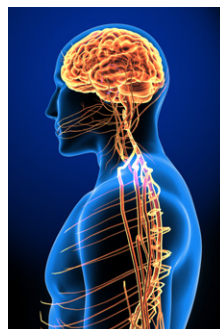


# THE HEALING POWER OF THE ENDOCANNABINOID SYSTEM

MICHAEL T. MURRAY, ND  
GIOVANNI APPENDINO, PhD  
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## THE SECRET TO FINDING BLISS AND BALANCE

can be found in the 600-million-year-old healing secret known as the endocannabinoid system. The scientific discoveries associated with this ancient healing system can help unlock ultimate wellness in a very profound way. Everything from brain function to the immune system to mental health is influenced by the endocannabinoid system. By supporting this internal complex network with diet, lifestyle and dietary supplements, we can heal from illness and achieve optimal health. This booklet is written by leading experts in the field of integrative medicine and features the latest scientific information in this exciting area of research. Enjoy this exploration of the healing power of the endocannabinoid system.



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