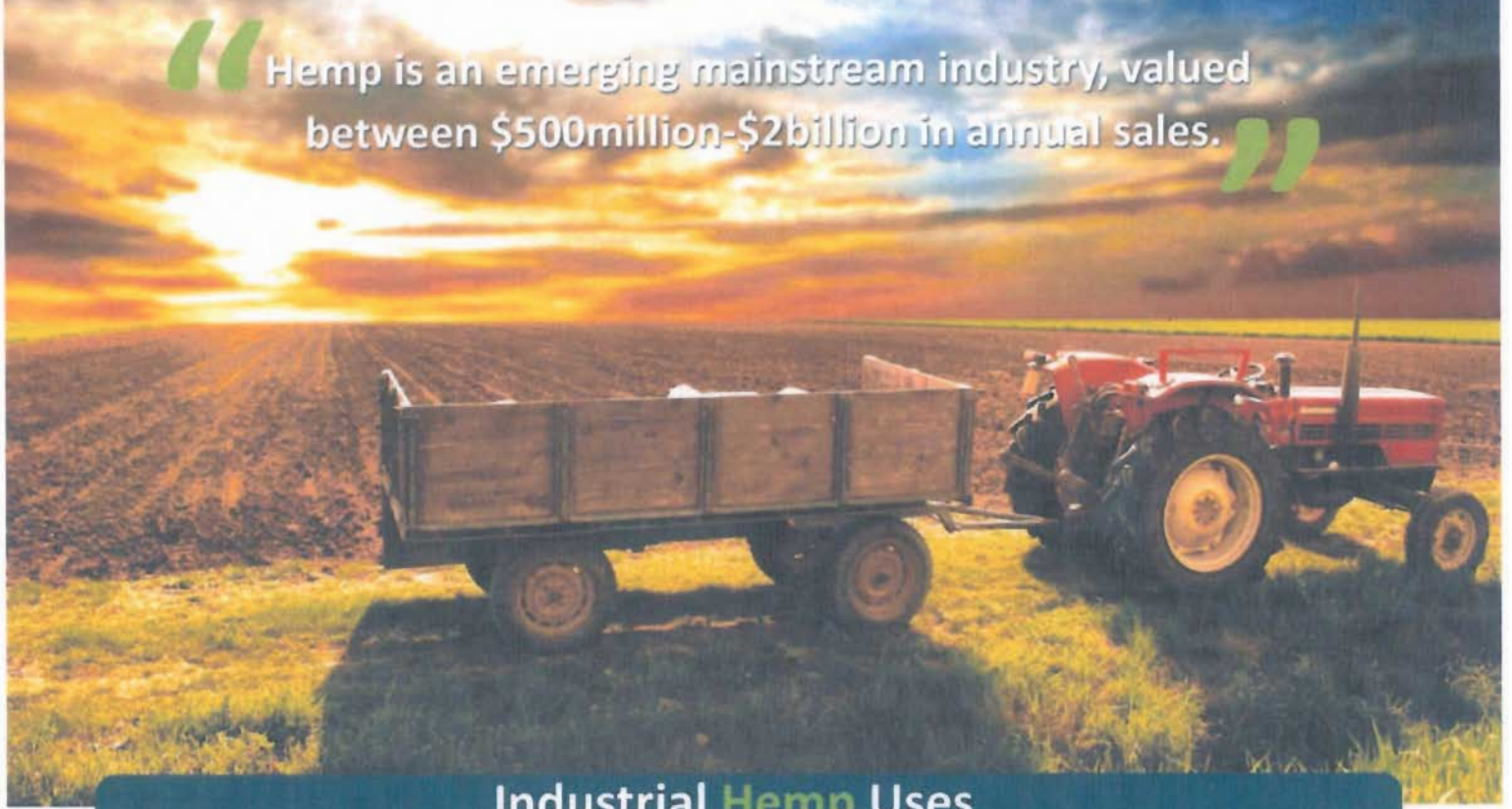
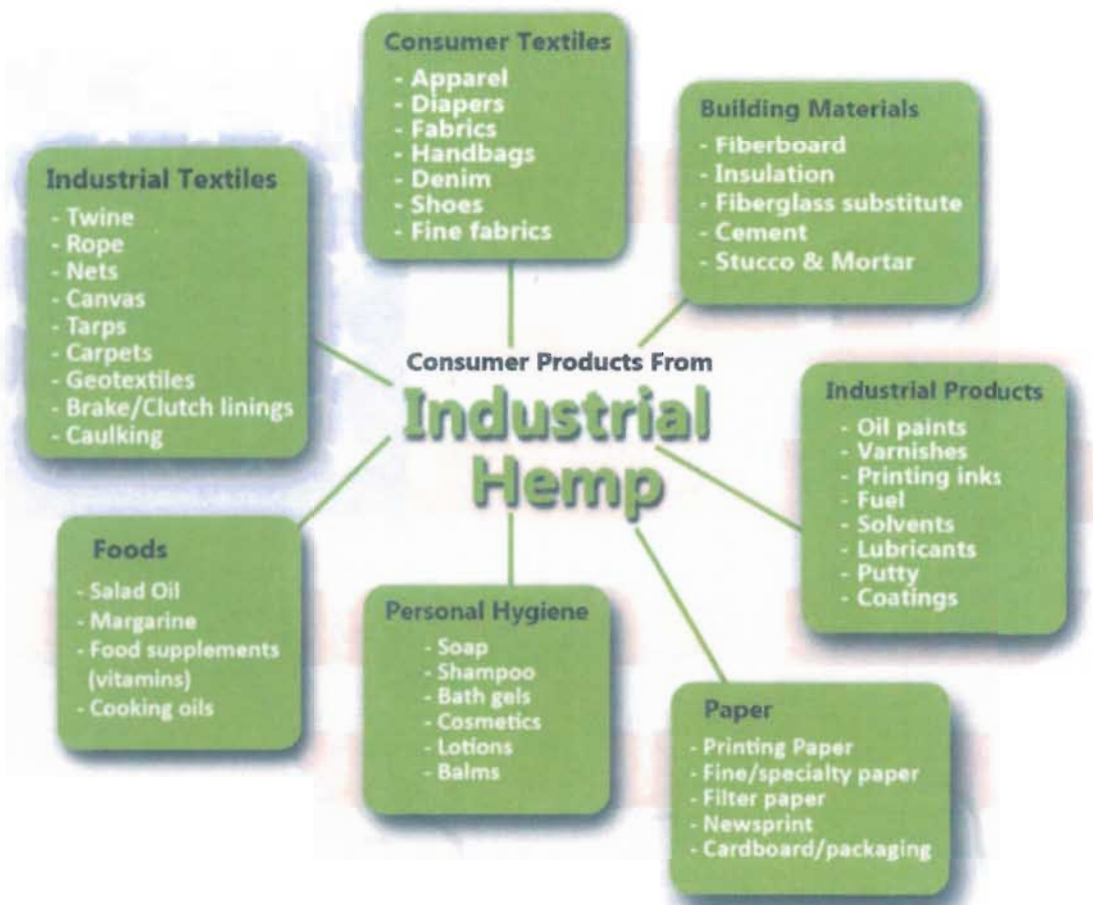


“Hemp is an emerging mainstream industry, valued between \$500million-\$2billion in annual sales.”



Industrial Hemp Uses



Invest In A Greener Future...

CBD

Information

Hemp and Your Body

Cannabinoids (CBDs) are chemical compounds in hemp that provide relief of pain, nausea, inflammation and more by imitating compounds our bodies naturally produce, called endocannabinoids (eCBD), which activate to maintain internal stability and health.

Simply put, CBD's mediate communication between cells, and when there is a deficiency or problem with our endocannabinoid system, unpleasant symptoms and physical complications occur.

Neurological:

Tinnitus, Epilepsy, Seizures, Spasticity, MS, Parkinson's, Alzheimer's

Mood:

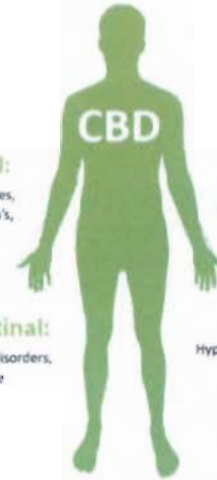
Stress, PTSD, PMS, Depression, Bipolar, Anxiety

Gastrointestinal:

Anorexia, Nausea, GI Disorders, Crohn's Disease

Other:

Hypertension, Lupus, HIV/AIDS, Muscular Dystrophy, Cancer

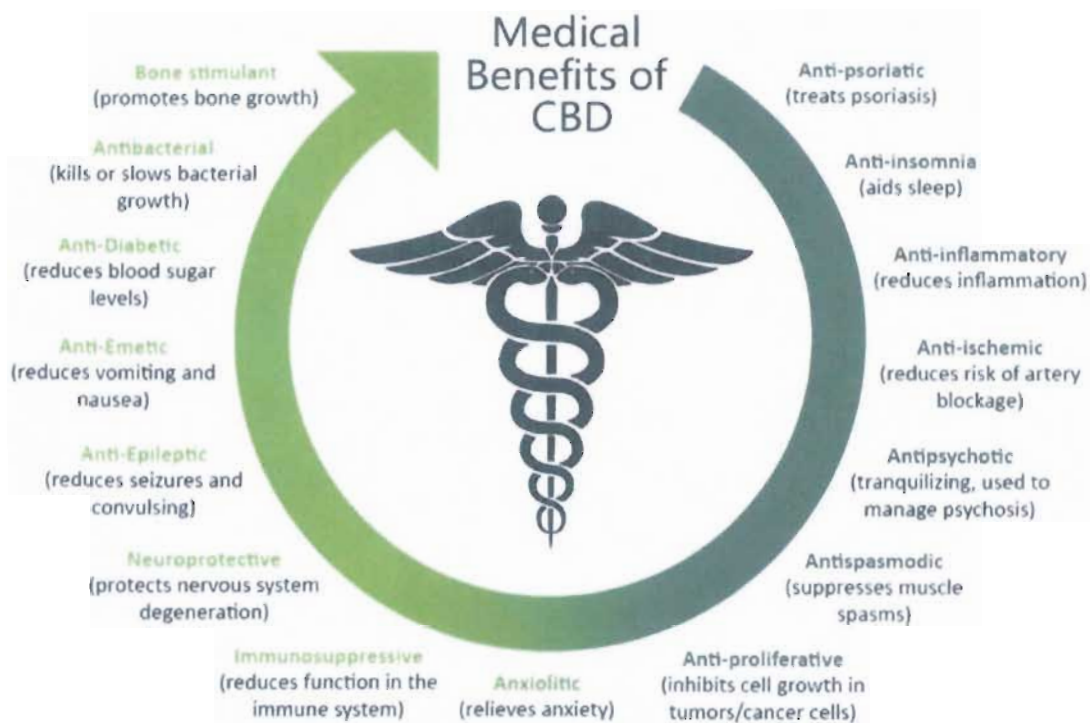


Relieves PAIN/Aids SLEEP: (Analgesic)

Arthritis, Inflammation, Muscle Spasms, Fibromyalgia, Phantom Limb, Spinal Injury, Insomnia, Migraine

Cannabinoid Receptors

There are two types of cannabinoid receptors in the body -- the CB1 receptors found primarily in the brain and the central nervous system, and the CB2 receptors that are distributed but primarily found in the immune system. These receptors respond to cannabinoids, whether they are from breast milk, or from a hemp plant.



CBD

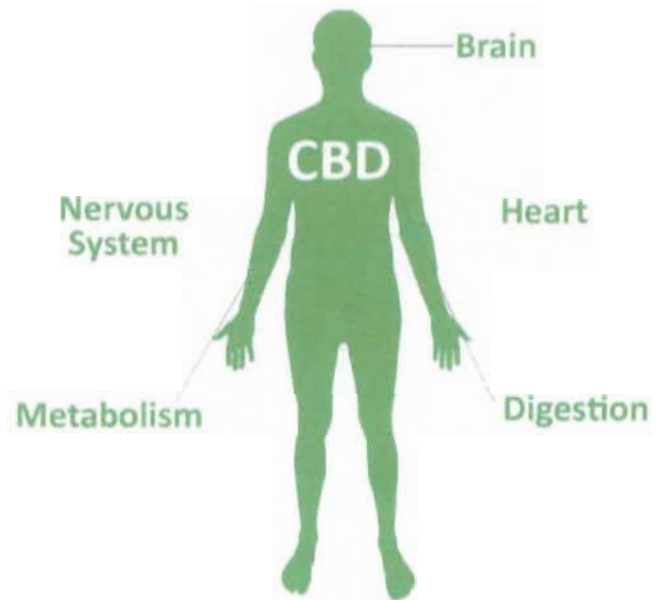
Information

CBD and Your Body

CBD - IT'S ABOUT LIVING HEALTHY, NOT HIGH.

Even though it seems like cannabidiol (CBD) is something new, it has been used by humans since the dawn of civilization. CBD is a natural constituent of cannabis, a plant that has been utilized for centuries as medicine. But CBD itself was only identified in the 1930s and 1940s, and its specific chemical structure was not documented until 1963. The research didn't end there; many scientists now consider CBD to be the single most important cannabinoid ever discovered.

Non-psychoactive CBD is a cannabidiol superstar. CBD is overwhelmingly responsible for many of the health and wellness benefits of the industrial hemp plant. And new benefits are being discovered all the time.

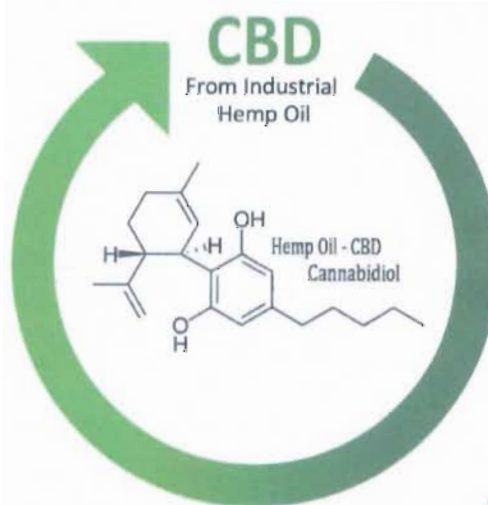


Cannabinoid Receptors

There are two types of cannabinoid receptors in the body -- the CB1 receptors found primarily in the brain and the central nervous system, and the CB2 receptors that are distributed but primarily found in the immune system. These receptors interact with cannabidiol and cannabinoids, made by the human body, or from industrial hemp rich in CBD.

My involvement with the field of cannabinoids, including CBD, spans close to three decades and covers a major part of my scientific career. During this period of time, I have witnessed the growth of modern cannabinoid biology, starting from the discovery of its two receptors: CB1 and CB2. I was fortunate enough to start at the beginning of this new era, and participate in a number of the new discoveries. It has been a very exciting journey. I have recently accepted a position to lead the Scientific Advisory Board for CannaVest™ Laboratories, a division of CannaVest Corp., and the producers of the award winning PlusCBD Oil™. We must educate the world about the amazing potential CBD holds for human and animal health."

- **Professor Alexandros Makriyannis**
Director, Center for Drug Discovery



"Now that we are producing unparalleled CBD formulas derived from industrial hemp, as opposed to marijuana, my personal mission is to identify the precise mechanisms of action for cannabidiol (CBD), and how that translates into noted health benefits. Oversimplification has dominated the commercial marketing of these products, and I am committed to elucidating the pluripotent actions of these remarkable plant compounds."

- **Dr. Joshua Hartsel**
CannaVest Laboratories

PLUS
+CBDoil
A Division of CannaVest Corp.

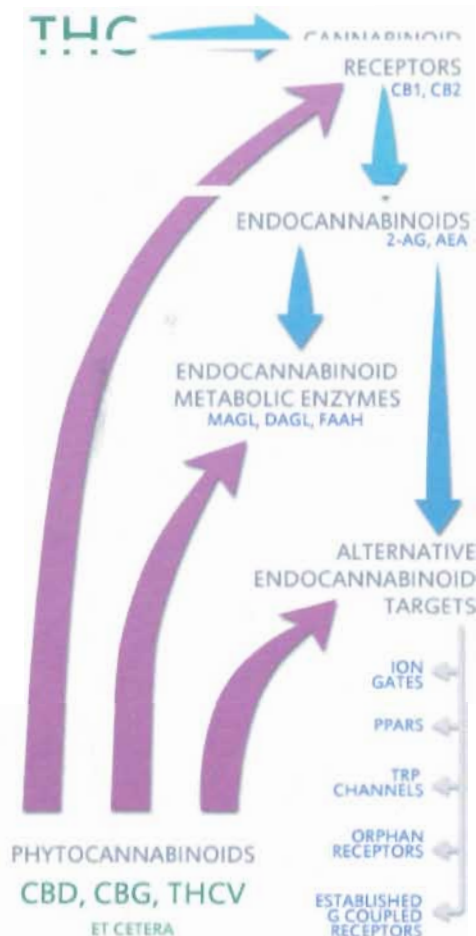
Research History

The dawn of cannabinoid science....

Despite the medicinal and recreational use of Cannabis for centuries, the identity of its main psychotropic constituent remained unknown until 1964 when Raphael Mechoulam, Yechiel Gaoni, and Habib Edery from the Weizmann Institute of Science in Rehovot, Israel, isolated and synthesised tetrahydrocannabinol (THC). It was subsequently established that this compound is responsible for the psychotropic effects of the plant, one early hypothesis being that since THC is so hydrophobic it induces these effects by interacting with cell membrane lipids. However as more was learnt about the pharmacology of THC and of synthetic cannabinoids such as CP55940 that induce THC-like effects it became increasingly likely that these effects must be mediated by a distinct family of receptors.

The discovery of cannabinoid receptors....

It was not until 1988 during experiments using radiolabelled CP55940 that the first of these receptors was actually identified. Aptly named cannabinoid receptor type 1 (CB1) it was located at the synapses of the central nervous system and importantly, the peripheral terminals of sensory neurones. CB1 receptors are thought to be the most widely expressed G protein-coupled receptors in the brain but are also found in peripheral tissues including peripheral nerves and non-neuronal tissues such as muscle, liver and fat. A few years later a second receptor (CB2) was identified through homology cloning. This is predominantly expressed in the cells of the immune system.



A receptor requires a ligand...

The discovery of cannabinoid receptors prompted the hypothesis that the body must produce one or more endogenous ligands (naturally occurring molecules) that bind to the receptor. The first such endogenous compound was isolated in 1992, just two years after the cloning of the CB1 receptor. This was the endogenous cannabinoid (endocannabinoid) anandamide (AEA) and investigators have shown that it functions as a CB1 receptor partial agonist. A second endocannabinoid, 2-arachidonoyl glycerol (2-AG), was discovered a couple of years later and in the following decade several other endogenous molecules that can activate CB receptors were identified. Evidence also emerged that the endocannabinoid system is transiently activated under certain stressful conditions to restore homeostasis.

Ligand biosynthesis and degradation...

Once endogenous cannabinoids were identified it was possible to demonstrate that they are removed from their sites of action by cellular uptake processes and to identify the intracellular enzymes responsible for both their production and metabolic degradation. Diacylglycerol lipase (DAGL) is a key enzyme in the biosynthesis of the 2-AG whereas

N-arachidonoylphosphatidylethanolamine-phospholipase D plays an integral role in the production of AEA. Both AEA and 2-AG are inactivated via ester bond hydrolysis and the primary enzymes responsible for these reactions are fatty acid amide hydrolase (FAAH) and monoacylglycerol lipase (MAGL) respectively. Endocannabinoid ligands are synthesized on demand rather than stored.

Manipulation of the endocannabinoid system...

There is now good evidence that the endocannabinoid system can be activated not only with compounds that directly target cannabinoid CB1 and/or CB2 receptors but also with inhibitors of endocannabinoid cellular uptake or of the intracellular metabolism of endocannabinoids by FAAH or MAGL. This has prompted a search for phytocannabinoids that can augment endocannabinoid levels by inhibiting these processes or indeed by activating biosynthetic enzymes such as DAGL in a manner that would enhance the protective role that increased endocannabinoid release plays in certain disorders.

Other endocannabinoid targets...

Interestingly, in some scenarios phytocannabinoids, synthetic cannabinoids and endocannabinoids are still able to induce certain effects even when the cannabinoid receptors have been blocked with an antagonist; evidence for the existence of non-CB receptor targets for these molecules. Further studies have demonstrated that these targets include transient receptor potential (TRP) channels such as TRPV1 and TRPM8, the peroxisome proliferator activated receptors (PPAR) alpha and gamma, G protein-coupled orphan receptors such as GRP55, certain ion channels (e.g. calcium channels), transmitter-gated ion channels (e.g. glycine receptors) and finally established non-cannabinoid G protein-coupled receptors (e.g. acetylcholine muscarinic receptors). We are now exploring the potential of phytocannabinoids to interact with targets other than CB1 or CB2 receptors in the search for therapeutically interesting pharmacology.

contributing authors: Prof Roger Pertwee & Prof Vincenzo Di Marzo

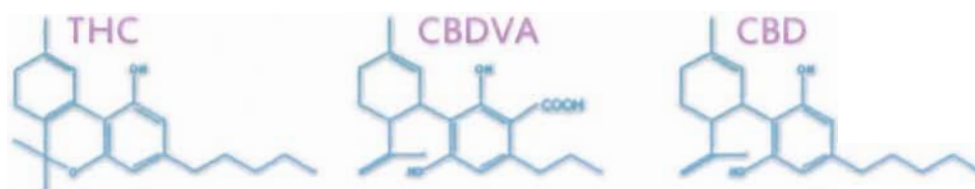
Cannabinoid Compounds

Phytocannabinoids, Endocannabinoids and Synthetic Cannabinoids

The term "cannabinoid" has different meanings. Cannabinoids were originally defined as a group of C₂₁ compounds uniquely produced by the cannabis plant. Subsequent development of synthetic cannabinoids and the discovery of natural cannabinoids in the body ("endocannabinoids") has somewhat blurred this definition. The molecules derived from the plant itself are therefore now termed "phytocannabinoids". Synthetic cannabinoids are those which have been man-made.

Phytocannabinoid Compounds

Naturally occurring cannabis (*Cannabis sativa*) contains a group of chemical compounds not found in other plants known as cannabinoids. Over 60 different cannabinoids have so far been identified but the role and importance of many of these has yet to be fully understood. GW is researching a large number of cannabinoids, each of which has different effects and applications.



GW has unique access to an extensive library of "phytocannabinoids" through the breeding of unique "chemotypes" (plants characterised by their chemical content). Currently available cannabinoids include:

D9-THC (Delta-9 Tetrahydrocannabinol)	CBDVA(Cannabidivarin - Acid)
D8-THC(Delta-8 Tetrahydrocannabinol)	CBC(Cannabichromene)
THCA(Tetrahydrocannabinol – Acid)	CBG(Cannabigerol)
THCV(Tetrahydrocannabivarin)	CBGA(Cannabigerol – Acid)
THCVA(Tetrahydrocannabivarin – Acid)	CBGV(Cannabigerovarin)
CBD(Cannabidiol)	CBN(Cannabinol)
CBDA(Cannabidiol - Acid)	CBNV(Cannabivarin)
CBDV(Cannabidivarin)	

Of the cannabinoids listed above, only two cannabinoids have to date been well characterized – THC and CBD. Both THC and CBD have important pharmacology: THC has analgesic, anti-spasmodic, anti-tremor, anti-inflammatory, appetite stimulant and anti-emetic properties, whilst CBD has anti-inflammatory, anti-convulsant, anti-psychotic, anti-oxidant, neuroprotective and immunomodulatory effects. CBD is not intoxicating and indeed it has been postulated that the presence of CBD in cannabis may alleviate some of the potentially unwanted side-effects of THC. There is currently limited scientific information on the pharmacology and toxicology of the other cannabinoids. Cannabinoids are believed to be effective in suppressing muscle spasticity, spasms, bladder dysfunction and pain symptoms of MS.

GW believes that the beneficial therapeutic effects of cannabis derived medicines result from the interaction of different

cannabinoids, hence GW's medicines consist of cannabinoids in different ratios. In addition GW believes that other components within the plant may also play a useful role.

Natural Cannabinoids (endocannabinoids)

The discovery of the cannabinoid receptors led to the demonstration of the existence of the body's own natural cannabinoids (endocannabinoids), the most important of which are arachidonoyl-ethanolamide (anandamide), 2-arachidonoyl glycerol (2-AG) and arachidonoyl glyceryl ether (noladin ether). This remains a highly dynamic field. There is evidence that anandamide can serve as a neuromodulator or neurotransmitter on its own or in conjunction with inactive precursors in what has been dubbed the "entourage effect".

Mechanism of Action

The Cannabinoid Receptor System

Only in the last two decades, a natural cannabinoid receptor system has been discovered in the human body. It is by interacting with these receptors that cannabinoids exert many of their pharmacological effects. The discovery of the cannabinoid receptor system has sparked renewed interest in the therapeutic potential of cannabinoids by providing important new targets for drugs. There are at least two types of cannabinoid receptors in mammalian tissues, CB1 and CB2. CB1 receptors are present in the brain and spinal cord and in certain peripheral tissues. CB2 receptors are expressed primarily in immune tissues. There is preliminary evidence to suggest that additional cannabinoid receptor types may exist.

Receptor Distribution

CB1 receptors are widely distributed but are particularly abundant in some areas of the brain including those concerned with movement and postural control, pain and sensory perception, memory, cognition, emotion, autonomic and endocrine functions. They are also found in appetite regulating areas such as the hypothalamus as well as reward centres such as the limbic system and have therefore been implicated in food intake. More recently, CB1 has been isolated in tissues that are important for energy metabolism such as the liver, adipose (fat) tissue and skeletal muscle. The second type of receptor, the CB2 receptor, can mediate regulation of cytokine release from immune cells and of immune cell migration in a manner that seems to reduce inflammation and certain kinds of pain.

So although the endocannabinoid system interacts with many neurotransmitter/neuromodulator systems it is important to note that phytocannabinoids have the ability to interact with all sorts of cellular pathways implicated in a range of diseases such as cancer and metabolic syndrome.

Receptor Modulation

Cannabinoids act as ligands (a small molecule able to dock onto the binding site of a protein) conferring their ability to modulate a receptor's behaviour and consequently their downstream biological pathways. Although the phytocannabinoids all have similar structures, they display a remarkably wide array of actions at each of the different receptors that are now thought to contribute to the endocannabinoid system (such as cannabinoid receptors, transient receptor potential [TRP] channels, melatonin and serotonin receptors, the PPARs and a host of orphan G-coupled receptors). For example it is known that THC positively regulates the CB1 receptor whereas it is negatively regulated by THCV; interestingly CBD has very little action at this site whatsoever.

It is important to note that terms positive and negative regulation can be broken down further into a range of subtle but important physiological actions.

Over the last few decades, when the pharmaceutical industry discover a receptor responsible for a particular disorder, they screen batteries of small molecules and compounds to identify any that could be used to treat that disorder. Often they have concentrated on those that exert the greatest effects, often referred to as full agonists or inverse agonists, in the hope that very small doses could lead to improved symptoms within patients in the clinic. Clearly there are circumstances where highly active compounds leading to absolute maximum or minimum receptor regulation may not offer the optimum pharmaceutical profile. In some families of receptors, especially those that have a constitutive activity, a partial agonist would offer a better solution. Endocannabinoids act as partial agonists, playing modulatory roles, and because phytocannabinoids behave in a similar fashion they can offer help within a dysregulated endocannabinoid system. GW are particularly well placed to explore these therapeutic advantages.

Positive Regulation:

This animation differentiates full agonists (usually synthetic compounds) and partial agonists (especially useful in systems such as the ECS which are under tonic control):



[CLICK HERE TO PLAY THIS ANIMATION](#)

Negative Regulation:

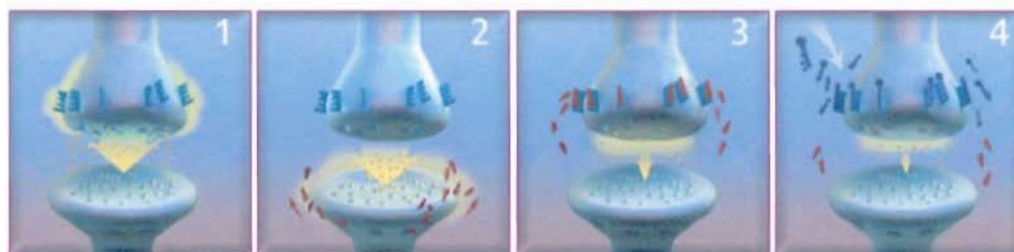
This animation illustrates the difference between inverse agonism and neutral antagonism at a constitutively active receptor:



[CLICK HERE TO PLAY THIS ANIMATION](#)

Regulation of Neurotransmission

As explained above, neurotransmitter modulation covers just one aspect of the mechanisms that govern cannabinoids therapeutic abilities. However as it was the focus of much early research within the field it is by far the most fully understood mechanism of action.



[1] Information is transmitted around the body in the form of electrical impulses that travel through nerves. As the signal reaches the end of the nerve, or axon, the resulting depolarisation stimulates the release of stored vesicles of neurotransmitters (the yellow molecules). These traverse the synapse (the gap dividing two nerves) where they bind to receptors on the post-synaptic cell. Activation of these post-synaptic receptors then initiates a series of events.

[2] One of these series of events is the release of Endocannabinoids (the red molecules) which are synthesised and released locally and function as a retrograde transmitter.

[3] The endocannabinoids travel in the opposite direction to the initial neurotransmitters, backwards across the synaptic cleft, and bind to pre-synaptic CB1 receptors (the light blue receptors). This feedback allows pre-synaptic regulation of transmitter release whereby the binding of endocannabinoids will retrogradely inhibit the release of further neurotransmitters, whether the neurotransmitters are inhibitory (e.g. GABA) or excitatory (e.g. glutamate)

[4] Phytocannabinoids are able to mimic the action of these endocannabinoids. In this way, they are able to augment the effect that endocannabinoids have in regulating the transmission of impulses from one nerve to another.

References:

Russo EB, Guy GW. A tale of two cannabinoids: the therapeutic rationale for combining tetrahydrocannabinol and cannabidiol. *Medical Hypotheses*. 2006;66(2):234-46.

Russo EB, Burnett A, Hall B, Parker KK. Agonistic properties of cannabidiol at 5-HT-1a receptors. *Neurochemical Research*. 2005;30(8):1037-43.

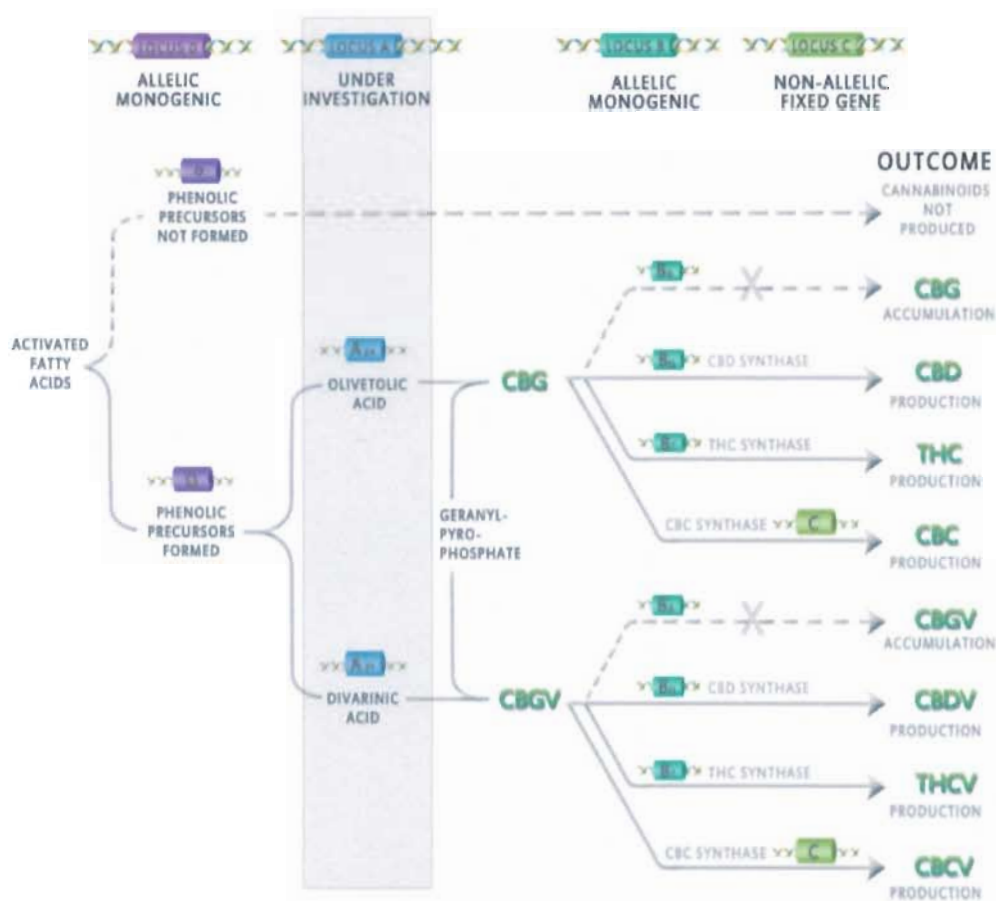
McPartland JM, Guy G. 2004. The evolution of Cannabis and coevolution with the cannabinoid receptor – a hypothesis. In: Guy, G.; Robson, R.; Strong, K.; Whittle, B. ed. *The Medicinal Use of Cannabis*, pp. 71-102. London: Royal Society of Pharmacists.

McPartland JM, Russo EB. Cannabis and cannabis extracts: Greater than the sum of their parts? *Journal of Cannabis Therapeutics*. 2001;1(3-4):103-32.

Cultivation

Breeding programme

GW's team includes experts in Cannabis breeding. In the genetic model used, the cannabinoid content of each chemical phenotype (chemotype) is controlled by four independent loci. By manipulating the genes at these four positions, our scientists can precisely control the cannabinoid composition of a plant. This is explained in the diagram below:



The gene at locus O allows the production of the initial phenolic precursors (resorcinolic acids). These combine with geranyl pyrophosphate to create the intermediate cannabinoids CBG and/or CBGV, the central precursors for the end-product cannabinoids THC(V), CBD(V) and CBC(V). The functional allele O is co-dominant; O/o hybrids have a low cannabinoid content and o/o plants are cannabinoid-free

The ratio of propyl- and pentyl cannabinoid precursors is determined by a postulated locus A, which is still under investigation.

The CBG/CBGV intermediate is further processed by the alleles of locus B. BD and BT are co-dominant; the BD gene converts CBG(V) into CBD(V) and the BT gene converts CBG(V) into THC(V). In the BD/BT genotype, codominance allows the expression of a mixed CBD/THC chemotype. Also at this locus, non-functional alleles, designated B0 can exist; these are unable to convert the CBG(V) intermediate and leave the plant with a CBG(V) predominant chemotype.

Locus C is fixed so all plants have CBC synthase activity. CBC synthase competes for the same CBG(V) precursor as the synthases encoded by locus B (THC and/or CBD synthase). In 'normal' Cannabis plants, CBC synthase is only active in the juvenile state. However, our scientists have discovered genetic factors that induce morphological mutations that are associated with a 'prolonged juvenile chemotype'. Prototype CBC production plants carry these factors in combination with B0/B0 at locus B. In these plants CBC synthase has no competition from THC or CBD synthase.

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Meijer EPM de, Bagatta M, Carboni A, Crucitti P, Cristiana Moliterni VM, Ranalli P, Mandolino G. 2003. The inheritance of chemical phenotype in Cannabis sativa L. *Genetics* 163: 335–346.

Meijer EPM de, Hammond KM. 2005. The inheritance of chemical phenotype in Cannabis sativa L. (II): cannabigerol predominant plants. *Euphytica* 145: 189-198.

Meijer EPM de, Hammond KM, Micheler M. 2009. The inheritance of chemical phenotype in Cannabis sativa L. (III): variation in cannabichromene proportion. *Euphytica* 165:293-311.

Meijer EPM de, Hammond KM, Sutton A. 2009. The inheritance of chemical phenotype in Cannabis sativa L. (IV): cannabinoid-free plants. *Euphytica* 168: 95-112.

Licensed and controlled cultivation

GW is licensed by the UK Home Office. Cultivation of GW's first Cannabis plants began in August 1998. Selected seedlings are maintained as clones. Clones are genetically identical, thus ensuring that the ratio of plant constituents is fixed within narrow limits. Clonal propagation does not involve genetic modification.

GW's botanical research team continues to develop new chemotypes. These will produce the raw material bases for future pharmaceutical research.

GW's Cannabis plants are grown in highly secure computer-controlled glasshouses. All aspects of the growing climate, including temperature, air change and photoperiod, are computer-controlled and the plants are grown without the use of pesticides. Careful control of the growing environment ensures that GW's plant material is grown to very strict pharmaceutical standards and that growth is phased to ensure continuity of supply.

Cultivation capability has been increased to cater both for commercial supply of our first product Sativex® and research quantities of novel chemotypes for the production of other medicines. Pharmaceutical production capacity has also been scaled up, both in-house and through external contractors, to supply tens of thousands of patients.

High levels of chemical consistency are important in applications made to medical regulatory authorities. Routine laboratory analysis demonstrates that GW's botanical raw materials meet strict specifications of quality.

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Potter D. 2004. "Growth and morphology of medical cannabis," pp. 17-54 in Guy G, Robson R, Strong K, Whittle B, eds. *The Medicinal Use of Cannabis*. Royal Society of Pharmacists, London.

McPartland JM, Clarke RC, Watson DP. 2000. *Hemp Diseases and Pests - Management and Biological Control*. CABI Publishing, Oxford University Press, UK. 251 pp.

Research Papers

Below are a range of selected publications within the fields of epilepsy, psychosis, metabolic syndrome and cancer that provide further pharmacologic background to these avenues of research:

Epilepsy

Report of a parent survey of cannabidiol-enriched cannabis use in pediatric treatment-resistant epilepsy.

Porter BE, Jacobson C. *Epilepsy Behav.* 2013 Dec;29(3):574-7

Cannabidivarin (CBDV) suppresses pentylenetetrazole (PTZ)-induced increases in epilepsy-related gene expression.

Amada N, Yamasaki Y, Williams CM, Whalley BJ. *PeerJ.* 2013 Nov 21;1:e214.

Cannabidivarin is anticonvulsant in mouse and rat.

Hill AJ, Mercier MS, Hill TD, Glyn SE, Jones NA, Yamasaki Y, Futamura T, Duncan M, Stott CG, Stephens GJ, Williams CM, Whalley BJ. *Br J Pharmacol.* 2012 Dec;167(8):1629-42.

Cannabidiol exerts anti-convulsant effects in animal models of temporal lobe and partial seizures

Jones NA, Glyn SE, Akiyama S, Hill TD, Hill AJ, Weston SE, Burnett MD, Yamasaki Y, Stephens GJ, Whalley BJ, Williams CM. *Seizure.* 2012 Jun;21(5):344-52

Phytocannabinoids as novel therapeutic agents in CNS disorders

Hill AJ, Williams CM, Whalley BJ, Stephens GJ. *Pharmacol Ther.* 2012 Jan;133(1):79-97

Δ^9 -Tetrahydrocannabivarin suppresses in vitro epileptiform and in vivo seizure activity in adult rats

Hill AJ, Weston SE, Jones NA, Smith I, Bevan SA, Williamson EM, Stephens GJ, Williams CM, Whalley BJ. *Epilepsia.* 2010 Aug;51(8):1522-32.

Cannabidiol displays antiepileptiform and antiseizure properties in vitro and in vivo

Jones NA, Hill AJ, Smith I, Bevan SA, Williams CM, Whalley BJ, Stephens GJ. *J Pharmacol Exp Ther.* 2010 Feb;332(2):569-77.

The phytocannabinoid Delta(9)-tetrahydrocannabivarin modulates inhibitory neurotransmission in the cerebellum

Ma YL, Weston SE, Whalley BJ, Stephens GJ. *Br J Pharmacol.* 2008 May;154(1):204-15.

Diabetes / Metabolic Disease

The cannabinoid $\Delta(9)$ -tetrahydrocannabivarin (THCV) ameliorates insulin sensitivity in two mouse models of obesity.

Wargent ET, Zaibi MS, Silvestri C, Hislop DC, Stocker CJ, Stott CG, Guy GW, Duncan M, Di Marzo V, Cawthorne MA. *Nutr Diabetes*. 2013 May 27;3:e68.

The endocannabinoid system in energy homeostasis and the etiopathology of metabolic disorders.

Silvestri C, Di Marzo V. *Cell Metab*. 2013 Apr 2;17(4):475-90

Cannabinoids and Endocannabinoids in Metabolic Disorders with Focus on Diabetes

Di Marzo V, Piscitelli F, Mechoulam R. *Handb Exp Pharmacol*. 2011;(203):75-104.

Cannabinoids inhibit insulin receptor signalling in pancreatic β -cells

Kim W, Doyle ME, Liu Z, Lao Q, Shin YK, Carlson OD, Kim HS, Thomas S, Napora JK, Lee EK, Moaddel R, Wang Y, Maudsley S, Martin B, Kulkarni RN, Egan JM. *Diabetes*. 2011 Apr;60(4):1198-209.

A role for the putative cannabinoid receptor GPR55 in the islets of Langerhans

Romero-Zerbo SY, Rafacho A, Díaz-Arteaga A, Suárez J, Quesada I, Imbernon M, Ross RA, Dieguez C, Rodríguez de Fonseca F, Nogueiras R, Nadal A, Bermúdez-Silva FJ. *J Endocrinol*. 2011 Nov;211(2):177-85.

Peripheral effects of the endocannabinoid system in energy homeostasis: adipose tissue, liver and skeletal muscle.

Silvestri C, Ligresti A, Di Marzo V. *Rev Endocr Metab Disord*. 2011 Sep;12(3):153-62.

Effect of dietary fat on endocannabinoids and related mediators: consequences on energy homeostasis, inflammation and mood.

Banni S, Di Marzo V. *Mol Nutr Food Res*. 2010 Jan;54(1):82-92.

Synthetic and plant-derived cannabinoid receptor antagonists show hypophagic properties in fasted and non-fasted mice.

Riedel G, Fadda P, McKillop-Smith S, Pertwee RG, Platt B, Robinson L. *Br J Pharmacol*. 2009 Apr;156(7):1154-66

Lifestyle-induced metabolic inflexibility and accelerated ageing syndrome: insulin resistance, friend or foe?

Nunn AV, Bell JD, Guy GW. *Nutr Metab (Lond)*. 2009 Apr 16;6:16.

Endocannabinoids, FOXO and the metabolic syndrome: redox, function and tipping point—the view from two systems.

Nunn AV, Guy GW, Bell JD. *Immunobiology*. 2010 Aug;215(8):617-28

The endocannabinoid system in metabolic control: a preface.

Di Marzo V. *Best Pract Res Clin Endocrinol Metab*. 2009 Feb;23(1):vii-ix.

Cannabidiol arrests onset of autoimmune diabetes in NOD mice.

Weiss L, Zeira M, Reich S, Slavin S, Raz I, Mechoulam R, Gallily R. *Neuropharmacology*. 2008 Jan;54(1):244-9

Cannabidiol lowers incidence of diabetes in non-obese diabetic mice.

Weiss L, Zeira M, Reich S, Har-Noy M, Mechoulam R, Slavin S, Gallily R. *Autoimmunity*. 2006 Mar;39(2):143-51.

Inflammation

Cannabidiol in inflammatory bowel diseases: a brief overview.

Esposito G, Filippis DD, Cirillo C, Iuvone T, Capoccia E, Scuderi C, Steardo A, Cuomo R, Steardo L. *Phytother Res*. 2013 May;27(5):633-6.

Beneficial effect of the non-psychotropic plant cannabinoid cannabigerol on experimental inflammatory bowel disease.

Borrelli F, Fasolino I, Romano B, Capasso R, Maiello F, Coppola D, Orlando P, Battista G, Pagano E, Di Marzo V, Izzo AA. *Biochem Pharmacol.* 2013 May 1;85(9):1306-16.

Cannabinoids mediate opposing effects on inflammation-induced intestinal permeability.

Alhamoruni A, Wright KL, Larvin M, O'Sullivan SE. *Br J Pharmacol.* 2012 Apr;165(8):2598-610.

Cannabinoid actions at TRPV channels: effects on TRPV3 and TRPV4 and their potential relevance to gastrointestinal inflammation.

De Petrocellis L, Orlando P, Moriello AS, Aviello G, Stott C, Izzo AA, Di Marzo V. *Acta Physiol (Oxf).* 2012 Feb;204(2):255-66.

Cannabidiol reduces intestinal inflammation through the control of neuroimmune axis.

De Filippis D, Esposito G, Cirillo C, Cipriano M, De Winter BY, Scuderi C, Sarnelli G, Cuomo R, Steardo L, De Man JG, Iuvone T. *PLoS One.* 2011;6(12):e28159.

Cannabis use amongst patients with inflammatory bowel disease.

Lal S, Prasad N, Ryan M, Tangri S, Silverberg MS, Gordon A, Steinhart H. *Eur J Gastroenterol Hepatol.* 2011 Oct;23(10):891-6.

Treatment of Crohn's disease with cannabis: an observational study.

Naftali T, Lev LB, Yablecovitch D, Half E, Konikoff FM. *Isr Med Assoc J.* 2011 Aug;13(8):455-8.

Impact of cannabis treatment on the quality of life, weight and clinical disease activity in inflammatory bowel disease patients: a pilot prospective study.

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PhD thesis, Dr David Potter

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