

International experts elaborate a consensus on the effects, present and potential medical utilities of cannabinoid based therapy

- According to healthcare experts, people most often don't differentiate well between cannabinoid based medicines and herbal cannabis, and they are not really aware of the risks of consuming the latter
- There is abundant clinical based evidence of the effects of cannabinoid based medicines, found in controlled clinical trials carried out with very strict conditions, but there is no such evidence for the herbal cannabis
- A cannabinoids experts broad review¹ of the effects and potential medical utilities of cannabinoid based medicines leading to a consensus recommendation was needed

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Over the last couple of decades there has been a significant growth in research efforts involving the human endocannabinoid (eCB) system, and experts have come a long way in identifying the cannabinoid human receptors, the internal molecules that interact with them and their possible changes in diseases. A panel of cannabinoids international experts have recently elaborated the consensus review "**Cannabinoids therapeutic use: what is our current understanding following the introduction of THC, THC:CBD oromucosal spray and others?**" which has been published online in the Expert Review of Clinical pharmacology journal¹, sponsored by the pharmaceutical company Almirall.

The aim of this consensus article is to review the most relevant scientific information available related to the medicinal use of different cannabinoids (natural or synthetic) for the treatment of human diseases, including tetrahydrocannabinol (THC), cannabidiol (CBD) and a number of other cannabinoids, to reflect the present and also the potential medical utilities of cannabinoid based therapy.

As stated by **Dr. Thomas Henze**, Passauer Wolf Reha-Zentrum, Nittenau, Germany, "*in the last few years a lot of scientific studies have been undertaken and published involving the use of cannabinoids as a medical drug and we should have a consensus on the efficacy of these drugs and compare it with other forms of cannabis treatments with herbal plants*".

Nevertheless, to a certain extent, people don't differentiate between cannabinoid based medicines and herbal cannabinoids. As explained by **Dr. Diego Centonze**, UOSD Multiple Sclerosis Clinical and Research Center, Tor Vergata University & Laboratory of Neuroimmunology and Synaptic Plasticity, CERC-Santa Lucia Foundation, Rome, Italy, "*I don't think people differentiate well between the cannabinoid based medicines and herbal cannabis. This confusion can be also seen in some healthcare professionals that tend to refer to cannabis as a whole without any differentiation between the different compounds, even in some published papers*".

Pharmacological research is expanding to investigate the role of the eCB system in diseases other than multiple sclerosis resistant spasticity, where THC+CBD oromucosal spray use is already approved, and nausea and vomiting or excessive weight loss (approved for synthetic THC), including various pain states, Alzheimer's disease, Parkinson's disease, Huntington's

disease, and epilepsy. According to the experts, in the next 5 years we will likely see a much greater focus on research aimed at identifying the link between the eCB system and specific pathologies. In the case of the cannabinoid based medicine THC+CBD oromucosal spray (Sativex®), indicated now for multiple sclerosis resistant spasticity, over the next 5 years, experts expect to get a clearer understanding of its overall benefits and safety, particularly when used for extended treatment periods and also effect on different spasticity or pain origins.

Clearly, one of the most important aspects relating to a scientific approach to medical use of cannabinoids is to fully establish the therapeutic benefits, safety and tolerability that each cannabinoid agent or combination possesses, so as to minimize the inappropriate use of products, aimed at achieving medicinal results, but containing different active principles with mixed properties. Findings with THC+CBD oromucosal spray are reassuring, and the same level of thoroughness needs to be applied to research with the different cannabinoid chemical entities in each disease setting that is being researched.

Is herbal cannabis comparable to cannabinoid based medicine?

As **Prof. Rafael Maldonado**, Laboratori de Neurofarmacologia, Departament de Ciències Experimentals i de la Salut (CEXS), Facultat de Ciències de la Salut i de la Vida, Universitat Pompeu Fabra, Barcelona, Spain has explained, *“there are big differences between an approved cannabinoid based medicine and herbal cannabinoids. In approved medicines, we know exactly which active compounds and excipients they contain, as well as the amount. But in the cannabis sativa plant there are more than 60 active compounds and we have no idea of the concentration of each of them. In addition, we have clinical based evidence of the efficacy of an approved medicine, found in controlled clinical trials carried out with very strict conditions. But we don't have it for the plant”*

Faced with this evidence, **Dr. Mauro Maccarone**, Department of Medicine, Campus Bio-Medico University of Rome; European Center for Brain Research/IRCCS Santa Lucia Foundation, Italy, has pointed out that *“we know that there is a major difference between cannabis based medicines and other substances, such as homeopathic products or herbal extracts. We really understand the active principles that are in cannabis based medicines and, therefore, we can try to take advantage of them so we know the amounts and the targets in our body. We have scientific knowledge, something that cannot always be said for homeopathic or general herbal products”*.

A variety of cannabinoid-based preparations with medicinal effects is currently available; some of them are approved for clinical use and are classified by origin as natural cannabinoids or synthetic cannabinoids. The route of administration of these preparations can be oral, sublingual/oromucosal, topical, smoked, or inhaled. Each compound or combination of compounds will have different pharmacokinetic properties and pharmacodynamic effects which would need to be tested in appropriate controlled studies. Among the approved ones, the global exposure of THC+CBD oromucosal spray (Sativex®) is estimated to be above 45,000 patient-years since it was given marketing approval for treating resistant spasticity in multiple sclerosis (MS) in 2011².

What are the possible consequences of consuming herbal cannabis?

The increase in the recreational consumption of cannabis sativa among adolescents and young adults is a cause for concern to health authorities and professionals working in the area of addiction given the association between continued use and academic failure³, problematic

behaviours⁴ and traffic accidents⁵. Furthermore, subsequent possible abuse and dependence on drugs such as cocaine or heroin⁶, and the possibility of depressive and psychotic episodes, are added concerns^{7,8,9}. Of particular concern are the possible future consequences of this consumption behaviour, both psychopathological and organic.

Unfortunately, most prevention programs implemented in the last couple of decades do not seem to have had a great effect on reducing recreational consumption of herbal cannabis. It might be a dramatic increase in the consumption of herbal cannabis in the years ahead, and it remains to be determined whether this will be limited to certain genetic-mediated “high-risk” groups of people¹⁰ and could decrease over time, or whether such uptake will spread further afield as was the case with tobacco in the last century¹¹.

There is sufficient scientific evidence to support the dangerousness of herbal cannabis in younger persons, and consumption might lead to a deterioration of basic psychic functions (attention, concentration and abstraction), difficulties in the construction and course of thought, paranoia and alteration of the sensory-perceptive processes, with hallucinatory phenomena and delusions¹².

As a conclusion, the complexity of the human endocannabinoid system is becoming better understood and there is abundant clinical based evidence of the effects (efficacy, tolerability...) of cannabinoid based medicines. Future research will likely focus on gaining a better understanding of the role of the eCB system in a number of diseases which could benefit for cannabinoid based therapy. At the same time, due to current legal developments for the consumption of cannabinoid based therapy in different countries, a greater number of patients might become eligible for these treatments.

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For more information, please visit www.almirall.com

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Media Contact

Cohn&Wolfe

Marta Gállego: marta.gallego@cohnwolfe.com; Tel. +34 91 531 42 67

Adriana Ibargüen: Adriana.ibarguen@cohnwolfe.com; Tel. +34 531 42 67