

High hopes for cannabinoids in MS

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CANNABINOIDS ARE THE ingredients found in the Cannabis sativa plant. The most extensively studied cannabinoid is delta-9-tetrahydrocannabinol (THC), which is the main ingredient underlying the psychoactivity associated with cannabis use. Further important cannabinoid components in the plant are cannabidiol and cannabinol, which make up proportions of the plant extract, but are not major contributors to the overall psychoactivity of cannabis use.

In addition to these "plant-derived" cannabinoids, a second major cannabinoid group incorporates the endogenous cannabinoids, or endocannabinoids, of which the most extensively studied are anandamide and 2-AG. Endocannabinoids are produced throughout the human body, and abundant levels are detected in both the nervous and immune systems. Both plant-derived and endogenous cannabinoids elicit diverse effects on the brain and on peripheral cells, tissues and organs, and these effects are mediated by cannabinoid receptors (CB1 and CB2), the expression of which has been determined on the cells of the nervous and immune systems.

The cannabinoid system is linked with all aspects of human physiology, and much research evidence indicates the therapeutic potential of this system. At the Department of Anatomy and Neuroscience in UCC our research, conducted in collaboration with Dr. Orna O'Toole (Mercy University Hospital), indicates that blood cells isolated from patients with MS, when compared directly with cells from healthy individuals, behave differently in terms of the inflammatory balance in the cell, which is heightened in MS. Interestingly, the lab's data demonstrate that plant-derived cannabinoids may uniquely target these inflammatory events, exerting



anti-inflammatory properties in peripheral cells from MS patients. This is important in not only improving our understanding of peripheral inflammatory changes that occur in individuals afflicted by MS, but may indicate how cannabinoid-based therapy, such as Sativex, may act to control the progression of the disease. Sativex is a combination of two plant-derived cannabinoids, THC and cannabidiol, which at the time of writing has been approved in over 20 countries for the relief of spasticity in patients with MS who have not responded adequately to other treatments.

Although Sativex dampens spasticity in MS, the specific mechanism by which this drug acts is uncertain. However, large bodies of research evidence back-up the therapeutic potential of both plant-derived and endogenous cannabinoid compounds, particularly in relation to the pathogenesis of MS. Indeed, cannabinoids can regulate the survival of nerve cells, possess anti-inflammatory properties, and can dampen the infiltration of immune cells into the nervous system, and hence reduce immune-mediated damage to nervous tissue. This may be promising for MS, but at present more research is needed, to determine the specific effects of cannabinoids in humans, and decipher exactly what happens to the endocannabinoid system in an individual with MS.

Cannabinoids are certainly unique compounds, and research supports their use as novel treatments. However, it is important to emphasize that Sativex is not cannabis; it is an oromucosal pump spray containing a combined cannabinoid medicine constituted by the two plant-derived cannabinoids, THC and cannabidiol in a 1:1 ratio. Interestingly clinical trial evidence for Sativex suggests that intoxication scores are low in patients. This is vital, as in order to gain broad support, cannabinoid-based therapies need to kick the drug of abuse stigma to the curb by remaining devoid of the classic cannabis-related psychotropic effects. With more research, cannabinoid researchers are coming closer to understanding and harnessing the beneficial effects of cannabinoids (plant-derived and endogenous), and on the way to doing so, bypassing the psychoactivity we classically associate with cannabis abuse.