My First Medical Writing

Editorial

After the debut of the first edition of this section, I was honoured to be contacted by many aspiring medical writers eager to contribute and to showcase their writing skills. Among them, Matías Rey-Carrizo did an amazing job in translating a complex and controversial topic into an enjoyable read. Matías has a PhD in medicinal chemistry and an extensive experience in scientific publications. After his last postdoctoral stay in Tokyo, he embarked on a medical writing journey as a freelancer at BCN Medical Writing. We hope you'll enjoy reading this article as much as we enjoyed creating it. If you're trying to get your foot in the door or know someone who is, don't hesitate and contact us!

SECTION EDITOR

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Cannabis's comeback:
New lessons from an old plant

In June 2018, the US FDA gave the green light to an oral solution of cannabidiol, the first drug containing a substance purified from cannabis.[1] To appreciate the magnitude of this announcement, let's recall the history of medicinal cannabis.

The term cannabis includes all plants of the genus *Cannabis*. Cannabis use has been documented since 4000 BC.[2] The plants have been cultivated for its fibres – so-called hemp – or for therapeutic purposes.[3] Cannabis's best studied medicinal properties include antiemetic, analgesic, anticonvulsant, and antimigraine effects.[3,4]

During the late nineteenth and early twentieth centuries, cannabis was included in Western pharmacopoeias, such as the British and American pharmacopoeias,[3] and several pharmaceutical companies (e.g. Merck, Bristol-Meyers Squibb, and Eli Lilly) were marketing cannabis extracts or tinctures.[5] However, cannabis was excluded from the American pharmacopoeia in 1941 because of the highly variable effects from different samples of the plant and the development of more effective medications (e.g. vaccines, aspirin, and barbiturates).[5] Most European countries followed the US lead in 1971.[4] In the 1960s, while the recreational use of the drug was soaring, the chemical structure of the main psychoactive ingredient, Δ^9-tetrahydrocannabinol (THC), was revealed.[6] The finding sparked a new interest in the therapeutic effects of the plant constituents and a spike in related publications. However, this increase was small compared to the one that occurred in 1988 with the discovery of the endocannabinoid system, composed of specific receptors in the nervous system sensitive to cannabis components[7,8] and a naturally occurring agonist, anandamide.[9]

To date, more than 460 compounds have been identified in cannabis, although only a handful are considered of therapeutic interest.[4] Until recently, the FDA had approved only two drugs derived from cannabis. The first, dronabinol, a synthetic form of THC, was licensed in 1985 as an appetite stimulant for people with AIDS and as an antiemetic for patients receiving chemotherapy.[10] The second, nabilone, a synthetic derivative of THC, was also approved in 1985 but was not marketed until 2006 and is indicated for chemotherapy-induced nausea and vomiting.[11] Further studies have revealed a potential for nabilone to treat chronic pain, for example, in multiple sclerosis.[12] Also noteworthy is nabiximols, an extract of cannabis containing THC and cannabidiol available in the UK and other Western countries, which is used for treating symptoms of multiple sclerosis, although this drug has not yet been approved in the US.[13]

Given the controversial matter of smoked medicinal cannabis, the trend has been to get away from natural preparations of unknown content and potency and, instead, develop drugs from isolated components with verifiable composition, stability, dosage, and pharmacology. For instance, when cannabidiol interacts with THC they produce variable outcomes.

Figure 1. Three species of the genus *Cannabis*.
From left to right: *Cannabis sativa*. Photograph by Thayne Tuason, distributed under CC BY-SA 4.0 licence. *Cannabis indica*. Photograph by Aleksander sowa (copyright free). *Cannabis ruderalis*. Photograph by Le.Loup. Gris, distributed under CC BY-SA 3.0 licence.

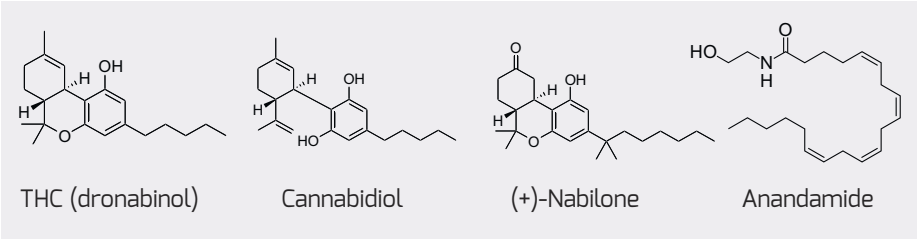

Figure 2. Chemical structures of Δ^9-tetrahydrocannabinol (THC) or dronabinol, cannabidiol, nabilone (a synthetic derivative of THC), and anandamide

Moreover, smoking cannabis or whole-plant extracts carries a risk of pulmonary damage or dependence, among other adverse effects.[14] Although there is evidence of the benefits of medicinal cannabis for chronic pain and for the palliative care of terminally ill patients, smoked cannabis is generally discouraged because of safety concerns, variable effects (preparation and interpersonal variabilities), and lack of quality control.[14,15,16]

In the US, until recently, the only approved drugs derived from cannabis were chemically synthesised. As mentioned above, this changed in June 2018 with the approval of cannabidiol, the main non-psychotropic constituent in *Cannabis sativa*.[1] Cannabidiol is structurally related to THC and interacts with the endocannabinoid system.[17] Clinical trials showed that cannabidiol reduces seizures in Dravet and Gastaut syndromes, two rare forms of epilepsy affecting children and infants.[18,19] As a result, cannabidiol was the first treatment approved for the Dravet syndrome and as a complementary treatment for the Lennox-Gastaut syndrome.

As with smoked medicinal cannabis, the usage of cannabidiol oil is also controversial. Its products have variable content of the active ingredient and are not approved by any regulatory agency. However, these preparations have been used for epilepsy, cannabis dependence, epidermolysis bullosa (a skin disorder), anxiety and insomnia, among other conditions.[20,21,22,23]

Finally, thanks to the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH), approval of cannabinoids in one country may lead to more widespread approval. Thus, extraction or synthesis of molecules from this mystical plant may lead to a new approach to medicinal cannabis.

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