Signa Vitae

Cannabinoids: A new friend or just another pandemic?

DOI:10.22514/sv.2021.194

Chryssoula Karanastasi[1,*]

[1]Pain Palliative Care Center, Henry Dunant Hospital Center, Athens, Greece. * ckaranastasi@gmail.com

Cannabis is a plant, native to Greece, the cultivation of which was under the protection of the State up until 1957. In 1961, due to pressure exercised mainly by the US, the UN proceed with a ban on all products from any part of the plant, under the pretext of its psychotropic effects. It does appear, however, that the real purpose behind America's actions was an attempt to consolidate the cotton fiber market at the time which, until then, had been mainly serviced by the durable fabrics derived from the hemp plant (ex. sails, sacks and ropes) - an unwelcome competitor. However, all across the globe people had learned to appreciate the cannabis plant as a source of fiber, of medicine, and as well as a recreational and spiritual medium, thus any attempt at isolation was bound to meet with failure - such as was witnessed during alcohol prohibition that led to similar consequences: the illicit domestic production and continued use of a commodity people simply did not want to part with.

During this time, organic chemist Raphael Mechulam managed to isolate tetrahydrocannabinol as a molecule, while in the ‘80s he went on to discover that mammals produce substances that are chemically related to cannabinoids, called endocannabinoids, and more so; that there is a system of specific binding receptors for these substances. His discoveries rekindled the interest of the scientific community in the possible therapeutic uses of the cannabis plant. At the same time, there began to be reports from patients of a variety of benefits they were seeing from consuming cannabis in various forms. Unfortunately, the legal framework for conducting integrated research in this area is complex, due to the limitations and regulations put in place that continue, to a great extent, until today. An additional complication is that the plant produces more than 150 chemical molecules that are identified today as cannabinoids, the actions of which are interconnected and interdependent, with clinical results contributed to by the terpenes and flavonoids that are also abundant in the plant. Therefore, designing a prospective study is seemingly mathematically impossible as the potential combinations of active molecules are plausibly infinite. In an attempt to side step these difficulties, the industry created synthetic replicas/equivalents of tetrahydrocannabinol, which were marketed as pharmaceuticals and tested in numerous clinical situations. Unfortunately, the resulting effects were disappointing - proponents of the plant attribute this to the absence of other molecules of cannabinoids, as well as terpenes and flavonoids, which have been shown to contribute to the therapeutic effects of cannabis (commonly known as the ‘entourage effect’).

Nonetheless, in countries such as Canada, with many states of Europe and the US following suit, patient appeals and the findings from various small-scale clinical trials were taken into consideration and a structured framework for prescribing and using cannabinoids for the treatment of a variety of symptoms has been established, usually in cases resistant to available medications. These include spasticity and pain that accompany multiple sclerosis, cachexia and refractory pain in cancer, nausea and vomiting from chemotherapy and neuropathic pain in HIV/AIDS. Several of the above indications have been adopted in our country since 2018: initially, following a recommendation by the Working Group of members of the Hellenic Anaesthesiology Society for the establishment of Therapeutic Protocols for painful syndromes, cannabinoid drugs were recognized as possible therapeutic options. Following this a special committee formed by the National Pharmaceutical Organization of Greece prepared the Core SmPC applicable to the marketing licence that must be applied for.

The current legal framework in Greece considers cannabis products to be included in schedule IV of the controlled substances list, meaning access is legal only with a Special Prescription for controlled substances. The molecule which is responsible for the inclusion of cannabinoid medications in schedule IV is Δ9-tetrahydrocannabinol. Many of the other cannabinoids, chiefly cannabidiol, are widely available on the market as they are not considered to have psychotropic effects but are neither considered to be medications in the strict sense of the term. Therefore, they cannot be prescribed by a physician, the cost is not reimbursed by the State and, concurrently, their consumption is generally not supervised by a specialist. In addition, no application for licensing of a medicinal product has been submitted for approval to the NPO, to date. Three years prior, the Ministry of Health had allocated the sum of about 70,000 euros for the importation of a number of vials of the most famous cannabis medication. After various time consuming bureaucratic adventures, the medication finally appeared for a few short days on the electronic prescription platform and, before being able to be allotted to patients, expired and was disposed of accordingly. Currently, if a Greek patient wishes to obtain these medications, he has three options available: (a) legally through IFET (the regulatory board responsible for individual drug importation), a purely theoretical process as no patient application has been processed to date and illegally (b) through avenues that deal in preparations of dubious quality and unspecified chemical composition, or (c) by cultivating the plant themselves.

Cannabis is generally agreed to be quite safe - even within its so-called recreational use no deaths from overdose have ever been reported (provided it is not combined with alcohol or other substances that act on the central nervous system). Cannabis is a "new" medication - even under the stress of the coronavirus pandemic, governments continue to modify and relax the legal regulatory framework. Cannabis is a trend - as is sometimes the case with many miracle promising herbs. Cannabis is ‘in’ - people around the world are turning to it not only for its therapeutic value but also for its textile and industrial applications. Cannabis is everywhere, and everyone wants to use it. However, the use of products of questionable

composition, home-cultivation and the unsupervised availability of cannabinoids expose patients to many risks: the most "innocent" is the use of excessively large doses of cannabidiol, which without a properly titrated dose, could possibly worsen the symptom which it is expected to relieve. A more substantial risk is the use of products that contain impurities, such as neem - an herbal pesticide that is thought to be responsible for the appearance of nausea and vomiting due to neurotoxicity. Other possible risks include being exposed to drug trafficking, the grey zone illegalities of cultivation and "use".

Cannabis is a plant, but it is also a chemical treasure trove. In western medicine, we are not trained to the pharmaceutical use of plants. Cannabinoids are medicinal substances that, despite the complicated difficulties that arise when we attempt to manage them as we would other regulated medications, must be treated as such. If we really want to take advantage of their therapeutic properties, we must administer them with the same responsibility that we bear for all medicines. Unregulated use of antibiotics has led to the emergence of drug resistant germs, while reckless over-prescribing has resulted in the recent opioid crisis. The "solution" offered by benzodiazepines has led many elderly, and not only, to dangerous withdrawal syndromes while in the past, amphetamines that were the recipe for success for students (and the obese) caused many deaths from cardiac complications. As doctors we have an obligation to our patients to act always with the aim of safeguarding their life and health - as is stated in the Code of Medical Ethics. There is no magic cure, nor are there any "innocent" drugs. In Greek, the word for medicine is the same as that for poison: rational use is what makes all the difference.

Let us thus be prudent, and not expect miracles – then, quite possibly, we may make way for them to happen.

References

[1] Abuhasira R, Shbiro L, Landschaft Y. Medical use of cannabis and cannabinoids containing products - Regulations in Europe and North America. European Journal of Internal Medicine. 2018; 49: 2–6.

[2] Häuser W, Finn DP, Kalso E, Krcevski-Skvarc N, Kress H, Morlion B, et al. European Pain Federation (EFIC) position paper on appropriate use of cannabis-based medicines and medical cannabis for chronic pain management. European Journal of Pain (London, England). 2018; 22: 1547–1564.

[3] Cannabisnews.gr