ACADÉMIE NATIONALE DE MÉDECINE

Académie nationale de Pharmacie

THERAPEUTIC EFFICACY OF CANNABIS?
Demonstrating its truthfulness with clinical trials that follow the rules of current good practices remains imperative.

Press release from the French National Academy of Medicine and the Academy of Pharmacy of March 14, 2022 [1]

An ongoing experiment (2021-2023) on the so-called "therapeutic" cannabis has been proposed, in a very exceptional way, by a specialized scientific committee; it has been validated by the French National Agency for the Safety of Medicines and Health Products. It concerns five pathologies: pain refractory to available therapies; some of severe and drug-resistant epilepsy forms supportive care in oncology; palliative situations; painful spasticity in multiple sclerosis.

The French National Academies of Medicine and Pharmacy recall that the current experimentation intended to justify the therapeutic use of cannabis derogates from the, safety and ethical methodological requirements governing the evaluation of any drug[1] candidate. A decree of October 16, 2020, which defines the specifications of cannabis-based medicines", exempts them from a randomized clinical trial, even though we know it is the only way to assess satisfactorily the benefit/risk balance of a drug candidate in the interest of patients. Another anomaly is linked to the fact that the experimentation does not concern pure substances, but products based on dried cannabis flowers and extracts with multiple components.

The National Academies of Medicine and Pharmacy point out that the benefit/risk balance has been assessed by randomized double-blind clinical trials for the two pharmaceutical specialties which have been granted a marketing authorization (MA). One, corresponding to pure cannabidiol, is on the market, whereas the other, which combines tetrahydrocannabinol with cannabidiol, is still not yet in France, 6 years after getting a MA, its medical service rendered being considered insignificant. Cannabinoids were used previously abroad in the treatment of pain, after randomized double-blind clinical trials, which led to positive conclusions. It is important, however, to take into account a recent meta-analysis of 32 such randomized clinical trials using medical cannabis or cannabinoids. The data included more than 5,000 patients with predominantly non cancer chronic pain. With moderate to high levels of evidence only a small to very small increase in the proportion of patients benefiting from a significant improvement in their pain, physical condition and quality of sleep was found at moderate to high levels of evidence. Adverse effects were either transient or increased beyond three months of treatment[2].
This meta-analysis only confirms data repeatedly reported in international analyses of neuropathic pain treatment, concluding that cannabinoids have a very low efficacy in chronic pain[3].
Regarding the evaluation of the therapeutic efficacy of potential medicinal products, a tri-academic press release[4] stated in 2020: "*In times of pandemic as well as in ordinary situations, the rules of the critical evaluation of methods and results must apply. The same applies to scientific and medical ethics, respect for scientific integrity and ethics in the reporting of results*". This position is in line with the opinion published in 2020 by the French National Center for Scientific Research: "*One can only worry that the choice of a treatment could be decided by public opinion on the basis of a petition or a poll and that political decisions could be taken on the basis of irrational beliefs or arguments, appealing only to fear or emotion*".

The Academies of Medicine and Pharmacy also point out that the global pharmaceutical industry has unsuccessfully tested many synthetic cannabinoids for analgesic and anti-inflammatory effects in recent years.
They consider that the ongoing experimentation on the possible therapeutic effects of cannabis should be free from media or political pressures that would mislead patients' expectations.

The Academies of Medicine and Pharmacy:
- consider it essential that the regulatory authorities (Agence Nationale de Sécurité Sanitaire du Médicament et des Produits de Santé and Haute Autorité de Santé) **be able**, in due course, **to analyze the data from clinical trial(s) in complete scientific independence** so that they can, as they usually do for any medicinal product, determine the benefit/risk balance as well as the medical service rendered and its improvement for patients.
- recommend, in the event that cannabis is made available for therapeutic purposes, that the monitoring of adverse effects and cases of abuse and/or diversion of use be ensured, as is the rule, by the Regional Pharmacovigilance Centres and Centres for Evaluation and Information on Drug Dependence-Addictovigilance.

1 – Press release of the National Academy of Pharmacy concerning the medical use of cannabis (November 24, 2020).
2 - Wang L et al: Medical cannabis or cannabinoids for chronic non-cancer and cancer related pain: a systematic review and meta-analysis of randomised clinical trials. BMJ 2021; 373: n1034. doi.org/10.1136/bmj.n1034.
3 - Stockings E et al: Cannabis and cannabinoids for the treatment of people with chronic noncancer pain conditions: a systematic review and meta-analysis of controlled and observational studies. Pain 2018:1932-1954. doi.org/10.1097/j.pain.(0)121293.
4 – Press release of the French National Academy of Medicine, the National Academy of Pharmacy, and the Academy of Sciences "Clinical trials during Covid-19 pandemic: therapeutic targets, methodological requirements, ethical imperatives" (May 29, 2020).
Je mettrais les acronymes français
Note: remember that two drugs, one CBD-based (Epidyolex®), the other consisting of a combination of THC and CBD (Sativex®) have “got” plutôt que “obtained” their marketing authorization in France under the usual conditions. Epidyolex® is prescribed as an adjuvant treatment for rare forms of epilepsy; although it has a high “medical service rendered” (SMR), it presents a minor improvement “of” plutôt que “in” this medical service (ASMR IV) compared to reference treatments. As for Sativex®, intended for a (et non the) adjunctive symptomatic treatment of the manifestations of spasticity linked to multiple sclerosis in patients insufficiently relieved by the reference antispasticity treatments, its SMR is low and its ASMR non-existent (ASMR V).

[1] Press release approved by the members of the Board of Directors.