

Marihuana and medicine: the debate persists

The ongoing public debate on the pros and cons of the medical use of marihuana and its possible declassification from the illicit drugs list refuses to cool down. For example, in the recent Israeli national elections, a new party was running on the single ticket of legalizing its recreational use (it did not receive enough votes to enter parliament). This mounting public interest has been the result of accumulating evidence of the effects of cannabinoids, the active ingredients of the cannabis plant, on human physiology. Evidence suggests that there might be several medical uses for cannabinoids, such as relieving chemotherapy and AIDS-associated nausea and wasting. Proponents for the medical use of cannabinoids have recently received support from the US Institute of Medicine's (IOM) recommendations, which suggest that clinical trials with cannabis products should proceed^{1,2}.

This book, which has an exceptionally broad scope, is therefore very timely. It takes the reader through diverse subjects, from the chemistry of the cannabis plant and of synthetic cannabinoid-mimetic drugs to the numerous physiological effects of cannabinoids on the human neuronal, cardiovascular, immune and reproductive systems, and to the sociological, ethnographic and historical perspectives of its use in various human cultures.

The text is logically organized into 12 sections; it begins with a superb historical review on marihuana and medicine from antiquity to present and leads to a discussion of the various aspects of the physiology and pharmacology of the cannabinoids. Among the pharmacological sections, of particular interest are contributions on cannabinoid geometry and biological activity (Chapter 1) and on the interaction of marihuana and its main active ingredient, Δ -9-tetrahydrocannabinol (THC), with other drugs (Chapter 19). Such interactions are important as people who abuse marihuana tend to abuse additional drugs.

Other noteworthy contributions pertain to the extensive study of cannabinoid use in pain relief, an area of huge therapeutic potential for both natural and synthetic cannabinoids (Chapters 38–48). This and other sections include previously published contributions, which give the reader a perspective on the accompanying studies. Other noteworthy themes include studies on the interaction of cannabinoids with brain-reward systems, which demonstrate that marihuana is just as habit-forming as other illicit drugs (Chapter 11), and studies on the amnesic effects of marihuana (Chapters 14–15).

Public health experts interested in marihuana policy will find in this book a fascinating depiction of the history of marihuana and its use in different cultures. Of particular interest is the discussion on the use of marihuana and alcohol in Islamic cultures, including a splendid translation of a 12th century Arabic poem that compares cannabis and alcohol (Chapter 63). Indeed, the forbidden use of alcohol in this culture has been a driving force behind the widespread use of cannabis in Asia and the Middle East.

Encompassing such diverse fields in a single volume is not simple (there are 79 contributions), so a few slips are forgivable. The most obvious flaw, however, does not seem to be an omission but a reflection of the editor's biased interest in the harmful effects of marihuana and THC. There is too little discussion of the therapeutic potential of marihuana or the cannabinoids in medicine, with the exception of its uses in glaucoma (Chapters 49 and 50) and AIDS-induced wasting (Chapters 60–62). The potential for treating chemotherapy-mediated anorexia with cannabinoids is only briefly discussed, and anorexia nervosa is not mentioned. A single contribution examines the potential use of cannabinoids in multiple sclerosis, but their potential for treating other autoimmune diseases is not discussed.

Another shortcoming is the lack of an extensive discussion on the recently discovered endogenous cannabinoids (endocannabinoids), anandamide and 2-arachidonoylglycerol (2-AG). These compounds are briefly mentioned in some of the contributions but deserve a more in-depth discussion. It is likely that future cannabinoid-mimetic drugs will not interact directly with cannabinoid receptors but will probably affect the pharmacokinetics of the endocannabinoids. By analogy, the only effective Alzheimer's disease remedy to date has come from acetylcholinesterase inhibitors, which elevate the levels of endogenously produced acetylcholine, rather than from natural or synthetic cholinergic agonists. Indeed, new studies suggest that certain fatty acid amides do not interact with cannabinoid receptors, yet exhibit potent cannabinoid-like activity by stabilizing endogenous anandamide and 2-AG (Ref. 3). It is plausible that among the many cannabinoid compounds in cannabis, some might affect the pharmacokinetics of the endocannabinoids, possibly prolonging their action. The recent IOM recommendations promote research on the biology of the endocannabinoids over and above paying, overly-conservative, attention to the biology of THC (Ref. 1).

The editors have assembled a remarkable synthesis of the many contributions in their General Conclusions section (Chapters 69–71). In closing, Gabriel Nahas delivers his verdict that 'marihuana or THC do not qualify as safe and effective medications... they have no place in modern Pharmacopeia from which cannabis was eliminated in the first part of the century.' Maybe this verdict is harsh, given our incomplete knowledge of the biology of cannabis and its many cannabinoids. A more refined conclusion should have left the door open for future studies on THC and other natural cannabinoids⁴. However, this book is a valuable addition to our knowledge and presents convincing evidence against the legalization of marihuana; at the same time it demonstrates how much more we need to learn about the physiology of the cannabinoids.

This book is a valuable tool for scholars interested in the controversy surrounding the medical potential of marihuana. Clinicians, pharmacologists, public policy makers and health-care workers should all benefit from the timely and well-presented information supplied here. Hopefully, it will stimulate further high-quality research on the remarkable biology of the cannabinoids.

Marihuana and Medicine

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