

VIEWPOINT

Cannabinoid research in the 2010s

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Cannabis sativa is possibly the plant with the longest history of cultivation by man (Russo, 2007). It has long been exploited for its fibre; as a biomass converter, it has exceptional utility. For most people, however, there is the association of cannabis with 'recreational drugs', which has led to the profusion of names associated with the plant and extracts thereof (marijuana, hashish, bhang, weed, grass, etc.). The 'modern' scientific era of cannabis research was prompted by the discovery of the major psychoactive ingredient in cannabis extracts (Gaoni and Mechoulam, 1964). This was, of course, Δ^9 -tetrahydrocannabinol or THC. Raphael Mechoulam has numerous publications, filled with seminal observations, including the identification of the two 'best' candidates for endogenous cannabinoid molecules: anandamide (Devane *et al.*, 1992) and 2-arachidonoylglycerol (Mechoulam *et al.*, 1995). He has become something of an icon in the cannabis field, with this issue of BJP containing a series of original articles prompted by a symposium held in Jerusalem in November 2010 to celebrate his 80th birthday. The first issue, entitled 'Cannabinoids in Biology and Medicine', containing primarily reviews, was published in August 2011 (<http://onlinelibrary.wiley.com/doi/10.1111/bph.2011.163.issue-7/issuetoc>). Current research in cannabinoid-related areas is vibrant, with the added focus of TRPV1 ion channels, PPAR nuclear receptors and the 'orphan' G-protein coupled receptors, GPR18, GPR55 and GPR119, as molecular targets of cannabinoids and cannabinoid-like molecules. Furthermore, the identification of endogenous agonists at cannabinoid receptors which lead to the demonstration of multiple routes for synthesis and transformation of these endocannabinoids has added to the molecular targets available for potential exploitation.

The involvement of 'big pharma' in cannabinoid research has been intermittent, with Pfizer and Sterling-Winthrop providing the very useful synthetic compounds CP55940 and WIN55212-2 in the 1970s and 1980s, respectively, without being able to translate these pharmacological successes into therapeutic solutions. The limiting factor for these compounds appears to have been the psychoactivity evoked

through activation of CNS CB₁ cannabinoid receptors. In the 2000s, Sanofi-Aventis achieved a measure of success with the CB₁ cannabinoid receptor antagonist/inverse agonist rimonabant (Acomplia®, SR141716A; Sanofi-Aventis, Paris, France) as one of the few pharmacotherapeutic alternatives for obesity. This success was short lived, however (approval was for 2006–2009 in Europe, not approved in the US), through adverse CNS effects in a significant minority of patients. In the clinical setting, therefore, cannabinoids are currently represented by THC itself (dronabinol, Marinol®; Solvay Pharmaceuticals, Brussels, Belgium), a THC analogue (nabilone, Cesamet®; Valeant Pharmaceuticals International, Mississauga, Canada) and THC in combination with other cannabinoids derived from the cannabis plant, notably cannabidiol (Sativex®; GW Pharmaceuticals, London, UK).

So where is cannabinoid research likely to go in the 2010s? The answer, as with many other fields of pharmacological/therapeutic interest, lies in the symposia and meetings focused on cannabinoids.

Cannabinoid symposia in the 2010s

Along with symposia on cannabinoids at the Winter meetings of the British Pharmacological Society, five major congresses have taken place since the summer of 2010:

- Conference on 'Cannabinoids in Biology and Medicine', organized by Dr Itai Bab in Jerusalem (Israel) to celebrate the 80th birthday of Dr Raphael Mechoulam, mentioned above
- 1st Course on 'Endocannabinoids', organized by Dr Daniele Piomelli within the Neuroscience School of Advanced Studies in San Quirico d'Orcia (Siena, Italy)
- Gordon Research Conference on 'Cannabinoid Function in the CNS', held in Les Diablerets (Switzerland) with Dr Beat Lutz and Dr Vincenzo Di Marzo as chairs
- The 'Cannabinoid Conference 2011', organized jointly by the International Association for Cannabinoid Medicines

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Linked Articles

This article is part of a themed section on Cannabinoids in Biology and Medicine. To view the other articles in this section visit <http://dx.doi.org/10.1111/bph.2012.165.issue-8>. To view Part I of Cannabinoids in Biology and Medicine visit <http://dx.doi.org/10.1111/bph.2011.163.issue-7>

(Dr Franjo Grotenhermen) and the European Workshop on Cannabinoids (Dr Andreas Zimmer) at the University of Bonn in Germany

- The 21st Annual Symposium of the International Cannabinoid Research Society (ICRS) was held in July 2011 in St. Charles (Illinois, USA)

As stated on the website (<http://www.cannabinoidsociety.org>), 'ICRS is . . . dedicated to scientific research in all fields of the cannabinoids, ranging from biochemical, chemical and physiological studies of the endogenous cannabinoid system to studies of the abuse potential of recreational *Cannabis*. . . the main role of the ICRS is to provide an open forum for researchers to meet and discuss their research.' Such a mission statement was once again a guideline in Pheasant Run, where ~250 delegates from all around the world discussed the most recent advances in the (endo)cannabinoid field. An important feature of the conference was the attendance by a large number of young scientists (~150 pre-doctoral and postdoctoral fellows); winners of the pre-doctoral Billy Martin Memorial Award and the postdoctoral J. Michael Walker Memorial Award were, respectively, Martin Sticht from the University of Guelph, Canada (presenting data on the use of a monoacylglycerol lipase inhibitor in studies of nausea-like and vomiting behaviours in shrews and rats), and Douglas McHugh from Indiana University, USA (presenting observations of the role of GPR18 in microglial function *in vitro*).

The scientific programme of the 21st ICRS conference included 60 oral presentations and 114 posters, divided into eight sessions covering the central and peripheral activities of (endo)cannabinoids: (i) learning, memory and pain; (ii) gastrointestinal and cancer; (iii) receptor signalling and structure; (iv) cardiovascular; (v) metabolism; (vi) neurobiology and neurodegenerative disorders; (vii) psychiatric; and (viii) cannabis, human use and addiction. The programme also featured the Symposium on 'Cannabinoids and HIV Pathogenicity' [chaired by Dr Vishnudutt Purohit and Dr Rao Rapaka from the National Institute on Drug Abuse (NIDA)], and two key lectures that added a special flavour to the field of (endo)cannabinoid research: the Presidential lecture on 'Huntingtin from Evolution to Pathology', delivered by Dr Elena Cattaneo (University of Milan, Italy), and the Kang Tsou Memorial lecture, delivered by Dr Sudansu K. Dey (University of Cincinnati, USA). In addition, the meeting hosted the very first continuing medical education course on 'Cannabinoids in Clinical Practice: Challenges and Opportunities' (organized by ICRS in collaboration with the Canadian Consortium for the Investigation of Cannabinoids, and the University of California at San Francisco), and the NIDA-

sponsored satellite Symposium on 'Endocannabinoid Metabolic Enzymes and Drug Development' (organized by Dr Rao Rapaka).

As usual, the overall quality of science was really high, with a personal selection of cutting edge topics discussed during the sessions (<http://www.icrs2011.org>): (i) the characterization of new lead compounds for the development of (full, partial or reverse) agonists/(neutral) antagonists of endocannabinoid-binding receptors, or inhibitors of their metabolic enzymes with potential therapeutic impact (e.g. for cancer, chemotherapy-induced pain, nausea and vomiting, or sleep-wake cycles); (ii) new NMR investigations into the structural properties of these receptors and metabolic enzymes, as well as into their interaction with membrane lipids and regulatory accessory proteins; and (iii) the identification of novel ω -3 fatty acid-derived ethanolamides that might complement (and even potentiate) the biological activity of more classical ω -6 fatty acid-derived endocannabinoids. These suggest that the ICRS still remains the reference forum where all aspects of (endo)cannabinoid research find a place. Therefore, we look forward to another successful year of cannabinoid meetings, particularly ICRS (<http://www.icrs2012.org>) in Freiburg, Germany.

Conflict of interest

MM and SPHA are Past-President and Secretary of ICRS, a nonprofit organization. Otherwise the authors state no conflict of interest.

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