Summary
Cannabis in India: Ancient lore and modern medicine
Ethan Russo

Cannabis has been employed medicinally in India for thousands of years. This chapter examines that usage in context of Ayurvedic (Hindu tradition of life and knowledge) and Unani (Arabic tradition) medicine, from the Sanskrit *Atharvaveda* of 1500 BCE, to its adoption by Western medicine in the 19th century, and its modern ethnobotanical usage on the subcontinent. The ancient texts are excerpted to provide illustrations of medical usage. The myriad historical therapeutic claims for cannabis are then examined in light of modern scientific biochemical and neuropathophysiological investigations, in context, which serve to support their rationale in the vast proportion. The history of cannabis provides a unique commentary on this medicinal phytomedicinal and how its pharmacognosy has led to a better fundamental understanding of our own neurochemistry and treatment of disease. This knowledge is leading to a renaissance of cannabis based medical therapeutics in the 21st century.

Key words: India, Ayurveda, Sanskrit, cannabis, ganja, THC, tetrahydrocannabinol, CBD, cannabidiol, herbal medicine, endocannabinoid

Cannabinoid chemistry: an overview
Lumír O. Hanuš and Raphael Mechoulam
(no summary and key words available)

Summary
Cannabidiol as a potential medicine
Roger G. Pertwee

The non-psychotropic plant cannabinoid, cannabidiol (CBD), has therapeutic potential for the treatment of epilepsy, anxiety, psychotic illnesses, central and peripheral inflammatory disorders, glaucoma and possibly also dystonia. It may also be effective against cancer and emesis and prove to be useful (1) for the management of Alzheimer's disease, sleep and appetite disorders, and neurotoxicity associated for example with stroke and (2) for attenuating unwanted side effects produced by Δ^9-tetrahydrocannabinol when this psychotropic plant cannabinoid is used as a medicine. This chapter reviews the preclinical and clinical evidence that supports each of these potential therapeutic applications of CBD.

Key words: cannabidiol, neurotransmission, epilepsy, Huntington's disease, dystonia, anxiety, schizophrenia, neuroprotection, inflammation, emesis, glaucoma, sleep, appetite, cancer, Alzheimer's disease,Δ^9-tetrahydrocannabinol

Summary
Mauro Maccarrone
Endocannabinoids and regulation of fertility

Available evidence clearly shows that in mammals endocannabinoid signalling is intimately associated with embryo-uterine interactions during implantation. The exact physiological siginificance of this signalling pathway is not yet clear, and it is not known how widespread it might be among different species. However, this review discusses the correlation between low FAAH in maternal lymphocytes and spontaneous abortion in humans, and presents converging evidence that suggests a major contribution of endocannabinoids to the hormone-cytokine networks responsible for embryo-uterine interactions. In addition, a novel interplay between progesterone, leptin, cytokines, FSH and the endocannabinoid-degrading enzyme FAAH (fatty acid amide hydrolase) is reviewed, pointing toward a key-role of this enzyme in controlling the endocannabinoid tone in reproductive organs. The perspective that factors able to enhance FAAH activity might become useful therapeutic tools for the treatment of male and female infertility in humans is also discussed.

Key words: ageing, apoptosis, embryo, Ikaros, implantation, leptin Leydig cells, lymphocytes, miscarriage, Sertoli cells, sex hormones, signal transduction, sperm, STAT3, uterus

Summary
Cannabinoids in neurodegeneration and neuroprotection
Javier Fernández-Ruiz, Sara González, Julián Romero and José Antonio Ramos

Cannabinoids have been proposed as clinically promising neuroprotective molecules, since they are capable to reduce excitotoxicity, calcium influx and oxidative injury. They are also able to decrease inflammation by acting on glial processes that regulate neuronal survival, and to restore blood supply to injured area by reducing the vasocontriction produced by several endothelium-derived factors. Through one or more of these processes, cannabinoids may provide neuroprotection in conditions of acute neurodegeneration, such as that occurring in traumatic injury or ischemic episodes, but also in chronic diseases affecting cognitive processes, such as Alzheimer's disease, motor control or performance, such as Parkinson's disease, Huntington's chorea and amyotrophic lateral sclerosis, or those initially produced by inflammatory processes, such as multiple sclerosis. Most of these diseases have been still scarcely explored for cannabinoid applications, but a rise in the number of studies should be expected in the future as soon as the promising expectatives generated for these molecules progresses from the present preclinical evidence to clinical applications.

Key words: cannabinoids, endocannabinoid signaling system, CB_1 receptors, CB_2 receptors, neurodegeneration, neuroprotection, excitotoxicity, inflammation, oxidative stress, ischemia, head trauma, Alzheimer's disease, Parkinson's disease, Huntington's disease, amyotrophic lateral sclerosis, multiple sclerosis

Role of the endocannabinoid system in learning and memory
Stephen A. Varvel and Aron H. Lichtman
(no summary and key words available)

Cannabinoids and anxiety
Richard E. Musty
(no summary and key words available)

Cannabinoid targets for pain therapeutics
Susan M. Huang and J. Michael Walker
(no summary and key words available)

Summary
Potential use of cannabimimetics in the treatment of cancer
Luciano De Petrocellis, Maurizio Bifulco, Alessia Ligresti and Vincenzo Di Marzo

The anti-neoplastic activity of THC and its analogues was first observed in the early 1970's, when neither cannabinoid receptors nor endocannabinoids had been discovered yet. Although these observations were of potential interest, no in-depth investigations were performed on this topic until a few years ago. By contrast, the beneficial effects of cannabinoids on some cancer-related disorders, such as emesis, nausea, muscle tension, insomnia, chronic pain, and loss of appetite, have been in part exploited pharmaceutically, since oral THC formulations can be prescribed legally in some countries for the treatment of nausea and emesis and as appetite-stimulating drugs for cancer and AIDS patients, respectively. We review here the results of recent studies suggesting that targeting the endocannabinoid system might provide a significant contribution to both palliative and curative cancer therapies. We also describe the molecular mechanisms through which plant, synthetic and endogenous cannabinoids exert their inhibition of tumor growth, and propose possible strategies for the use of cannabimimetics against cancer and some of its symptoms.

Key words: cannabinoids, endocannabinoids, anandamide, 2-arachidonoylglycerol, receptors, vanilloid, cancer, tumor, apoptosis, proliferation, cell cycle, growth factor

Summary
Cannabinoids: Effects on vomiting and nausea in animal models
Linda Parker, Cheryl L. Limebeer and Magdalena Kwiatkowska

The marijuana plant has been used for several centuries for nausea and vomiting; however, it is only since the mechanism of action of the psychoactive ingredient, Δ^9-tetrahydrocannabinol (Δ^9-THC), was discovered that research has provided experimental evidence for its effectiveness. Cannabinoids have been shown to reduce vomiting in cats, pigeons, ferrets, least shrews, *Cryptotis parva* and the house musk shrew, *Suncus murinus*. Although rats and mice do not vomit, they display a characteristic gaping reaction when intraorally infused with a flavor

previously paired with an emetic drug. This conditioned gaping reflex is believed to reflect conditioned nausea in this non-emetic species. Cannabinoid agonists have been shown to prevent the establishment of this conditioned gaping response in rats and interfere with the expression of previously established conditioned gaping responses in rats. Animal models have provided considerable evidence that cannabinoids are effective in reducing nausea and vomiting elicited by a wide range of toxins.

Key words: nausea, vomiting, shrew, gape, chemotherapy, cisplatin, lithium chloride, ferret, rat, emesis, anti-emetic, serotonin, anandamide, 2-AG, SR-141716, HU-210, CP 55, 940, WIN 55, 212-2, Δ^9-tetrahydrocannabinol, Δ^9-THC, cannabidiol, CBD, taste avoidance, taste aversion, conditioned rejection, taste reactivity

Summary
The skeleton: stone bones and stoned heads?
Itai A. Bab

Although the CB_2 receptor was cloned more than a decade ago, its physiological role remained elusive. Using a combined approach encompassing molecular and cellular biology, pharmacology and genetic analyses in mice and humans, we were able to show a role for CB_2 signaling in regulating bone mass. Furthermore, the novel association of polymorphisms in the human *CNR2* locus with osteoporosis and the attenuation of OVX-induced bone loss by a synthetic cannabinoid receptor agonist suggest that endocannabinoid signaling in bone remodeling is similar in mice and humans. The association with human osteoporosis around the *CNR2* coding region and the attenuation of the deleterious effects of OVX on bone by a peripherally selective CB_2 cannabinoid receptor agonist have major implications on osteoporosis, offering new molecular targets fo the diagnosis and treatment of this disease.
Still in line with the mouse findings, CB_1 is apparently not involved in age-related bone loss commonly diagnosed in humans, and may have an important role in early skeletal development.

Key words: bone, bone mass, bone loss, bone remodelling, bone resorption, bone formation, osteoblast, osteoclast, osteocyte, osteoporosis, CB_1-deficient mouse, CB_2-deficient mouse, HU-308, CB_2 specific agonist

Summary
Cannabinoids and drugs of abuse
Daniela Parolaro and Tiziana Rubino

Hemp plant derivatives, marijuan and hashish, are among the most widely abused drugs in humans. The potential ability of cannabis derivatives to produce dependence in humans is still a controversial issue although in recent years dependence on marijuana is increasingly gaining recognition as a clinically significant phenomenon. The existence of abuse liability of cannabinoids in animals is much more clearly observable. Several behavioral models have been use to evaluate tolerance and withdrawal, as well as the rewarding properties of cannabinoids, and to explore the molecular basis of cannabinoid dependence. Finally, the occurrence of the endocannabinoid system in the reward circuits and its role in motivational and emotional homeostasis suggests that it could be relevant in modulating the rewarding properties of other

drugs of addiction, opening a new therapeutic approach to the pharmacological treatment of addiction.

Summary
Cannabinoids in appetite and obesity
Francis Barth and Murielle Rinaldi-Carmona

Natural and synthetic cannabinoid agonists stimulate food consumption in animals and humans. Dronabinol, an oral formulation of Δ^9-THC, is used as a therapeutic agent to treat anorexia and cachexia associated with AIDS and cancer. Interestingly, recently discovered cannabinoid antagonists such as rimonabant display an opposite profile, selectively decreasing the intake of palatable food in animals. Moreover, clinical studies have demonstrated that rimonabant was able to decrease body weight and improve important cardiovascular risk factors in obese patients. These effects appears to be mediated by CB1 cannabinoid receptors located both in brain and in peripheral tissues such as adipocytes.

Geoffrey W. Guy and Colin G. Stott
The development of Sativex® – a natural cannabis-based medicine
(no summary and key words available)

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