Cannabinoids as Therapeutics
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Cannabinoid chemistry: an overview

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Introduction

Cannabis sativa probably originates from neolithic China [1]. However the exact period of its domestication is unknown. The first known record of the use of cannabis as a medicine was published in China 5000 years ago in the reign of the Emperor Chen Nung. It was recommended for malaria, constipation, rheumatic pains, absent-mindedness and female disorders. Later its use spread into India and other Asian countries, the Middle East, Asia, South Africa and South America. It was highly valued in medieval Europe. In Western Europe, particularly in England, cannabis was extensively used as a medicine during the 19th century, while in France it was mostly known as a "recreational" drug [2].

Natural cannabinoids

The first successful attempt to identify a typical cannabis constituent was achieved by Wood et al. [3], who isolated cannabinol from the exuded resin of Indian hemp (*charas*), which was analysed as $C_{21}H_{26}O_2$. Another big step was made by Cahn, who advanced the elucidation of the structure of cannabinol [4], leaving as uncertain only the positions of a hydroxyl and a pentyl group. Several years later Todd's group in the UK [5, 6] and independently Adam's group in the USA [7] synthesized several cannabinol isomers and compared them with the natural one. One of the synthetic isomers was identical to the natural product. The correct structure of the first natural cannabinoid, cannabinol, was thus finally elucidated. These two groups assumed that the psychotropically active constituents were tetrahydrocannabinols (THCs), which however they could not isolate in pure form and therefore they could not elucidate their structures.

A second cannabis constituent, the psychotropically inactive cannabidiol, was also isolated, but its structure was only partially clarified [8]. Synthetic THC derivatives, which showed cannabis-like activity in animal tests, were prepared, but they obviously differed from the active natural product, on the basis of their UV spectrum [9–12].