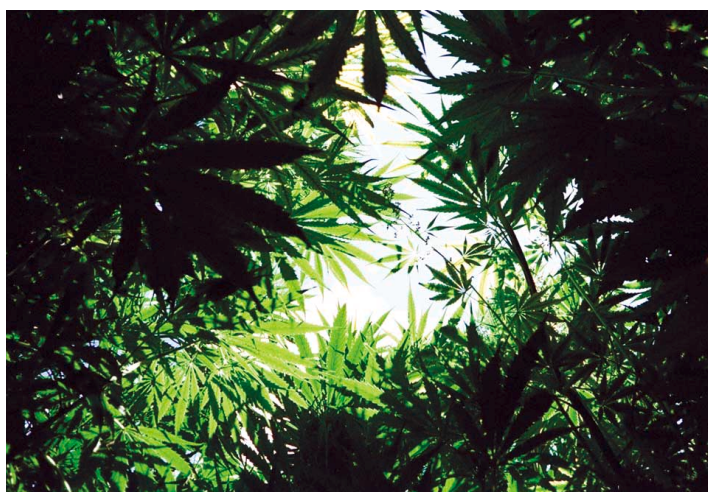


From soft drugs to legal medication

GCMS: The unusual product of an unusual company

THC Pharm is the first company in Europe to manufacture dronabinol (THC) and cannabidiol (CBD), the cramp and pain relieving main active compounds of the cannabis plant (hemp). These active compounds are available as prescription narcotics and are being used increasingly in the treatment of cramps, pain, nausea or lack of appetite. Purity testing and quality control of these products at THC Pharm is carried out using Shimadzu's GCMS systems.



Hemp – cultivated also as crop plant for hundreds of years

THC Pharm was founded in Frankfurt, Germany, in 1996 as a patient initiative of four friends and associates. The founders wanted to help provide patients who already had experienced positive therapeutic effects using illegal cannabis, to obtain the cannabis active compounds legally, in appropriate dosages and of pharmaceutically pure quality. An endeavour which met at first with enormous resistance from the public prosecution department and authorities in the course of an intensive drug debate, although at that time a similar but very expensive cannabinoid-based product already existed in the United States.

The many barriers that were overcome over time can be attributed to the dedication of the four partners which included Dr. Joachim Hartiger, left a quadriplegic after a car accident.

History of cannabis

Hemp has been known for many hundreds of years as a cultivated as well as a crop plant. Already in the fourth century B.C., hemp was cultivated in China, as the fibre-rich plant was highly suited for the manufacture of paper, textiles and ropes. In this function, the hemp plant also experienced a Golden Age in Europe and was used for instance as main raw material for the sails and ropes necessary in shipbuilding.

Cannabis was not only used in ancient Chinese medicine. The Egyptians, Assyrians and Indians also knew about the medicinal activity of hemp. It was administered mostly as pain medication and relaxant but was also used to treat loss of appetite and lower abdominal pain.

Today, hemp plays an important role in ayurvedic medicine due to its wide range of therapeutic applications.

In contrast, the medicinal use of hemp only became known in Europe in the 19th century. Soon thereafter, a variety of pain relieving tablets based on hemp became available. After World War II, the well-known medicinal plant was gradually displaced from the market by newly patented pain relievers. Today the use of the hemp plant or its constituents for self-medication or for recreational use is prohibited. In recent years, the low addiction risk of cannabis and its excellent tolerance has sparked a worldwide renaissance in medical research on cannabinoids. The objective nature of the discussion on the medicinal

advantages of cannabis has played an important role here. This development has, however not gone as far as with opiates, where virtually no associations are made anymore with opium pipes or heroin syringes.

Activity and application areas for dronabinol

The muscle relaxing, appetite stimulating, nausea inhibiting and pain relieving properties of cannabis products are well documented. In addition, there are the soothing, mood enhancing, bronchial dilating and inner eye pressure decreasing effects that are now being investigated in further research. In most therapeutic applications, combinations of these properties are of importance.

Since 1985, a cannabis product has been approved for prescription under the name of Marinol. It is used in the treatment of patients who suffer from nausea and vomiting due to chemotherapy and who do not respond well to any standard anti-nausea medication.

In recent years, another authorised indication for the use of cannabis has been the treatment of loss of appetite in AIDS patients. The import of fully synthetic Marinol from the USA is, however, time-consuming and expensive. In addition, this medication is only available in tablet form – a severe obstacle for severely ill patients who are suffering from nausea and vomiting or massive swallowing impairments.

Standardisation of the active compound content

For the founders of THC Pharm the pain and cramp relieving and therapeutic activity of dronabinol was most significant as it ♦



The highly sensitive quadrupole mass spectrometer GCMS-QP2010

allowed the quadriplegic Dr. Hartinger to lead a 'normal' life and to continue his scientific research. Furthermore, patients suffering from severe pain who have reached the end of the road in conventional therapy, multiple sclerosis patients and quadriplegic patients all benefit from this drug which has brought about a significant improvement in the quality of life and mobility – an experience that many patients had already made with illegal cannabis.

It is estimated that one third of severely ill MS- or quadriplegic patients are using illegal cannabis products in addition to their regular medication.

However, this practice has been made difficult and patients who rely on self-medication have had to get their hemp products on the black market.

The problem with products available on the black market is not just that they are illegal, but also the problematic dosage consistency, as the active compound content of the illegally traded plants varies strongly. In order to be useful as a medication, the active compound content must be standardised. It is obvious that the black market neither adheres to, nor guarantees any pharmaceutical criteria such as purity, stability and consistent quality.

GCMS identifies individual components

After founding the company in 1996, THC Pharm developed a process for extracting semi-synthetic THC (dronabinol) from fibre hemp. The cultivation of fibre hemp is legal and therefore poses no problems, as this type of

hemp only contains a very low amount of psychoactive THC and a concentration of up to ten times more of the very weakly psychoactive cannabidiols, which can be chemically converted into 99 % pure THC. Purity testing for the first experiments were initially carried out on a gas chromatograph with flame ionisation detection. An early problem was that no standards were available for the identification of the individual components of the reaction mixture. A used Shimadzu GCMS-QP-5000 gas chromatography-mass spectrometer was purchased and applied for the accurate identification of the individual components of the reaction mixture based on mass spectra. This instrument is still being used today at THC Pharm for quality control (Figure 1).

July 2000: Approval and permission

The synthetic- and QA procedure was established, however an application to obtain permission for the manufacture of a cannabis extract was turned down in 1997. In the beginning of 1998, dronabinol was available only on prescription in Germany as a narcotic. As pharmacies in Germany were allowed to prepare and dispense cannabis drugs in limited quantity, pharmacist and physician Christian Steup contacted a friend and pharmacist at the Bock Pharmacy in Frankfurt, Germany in order to prepare dronabinol according to his own procedure and to

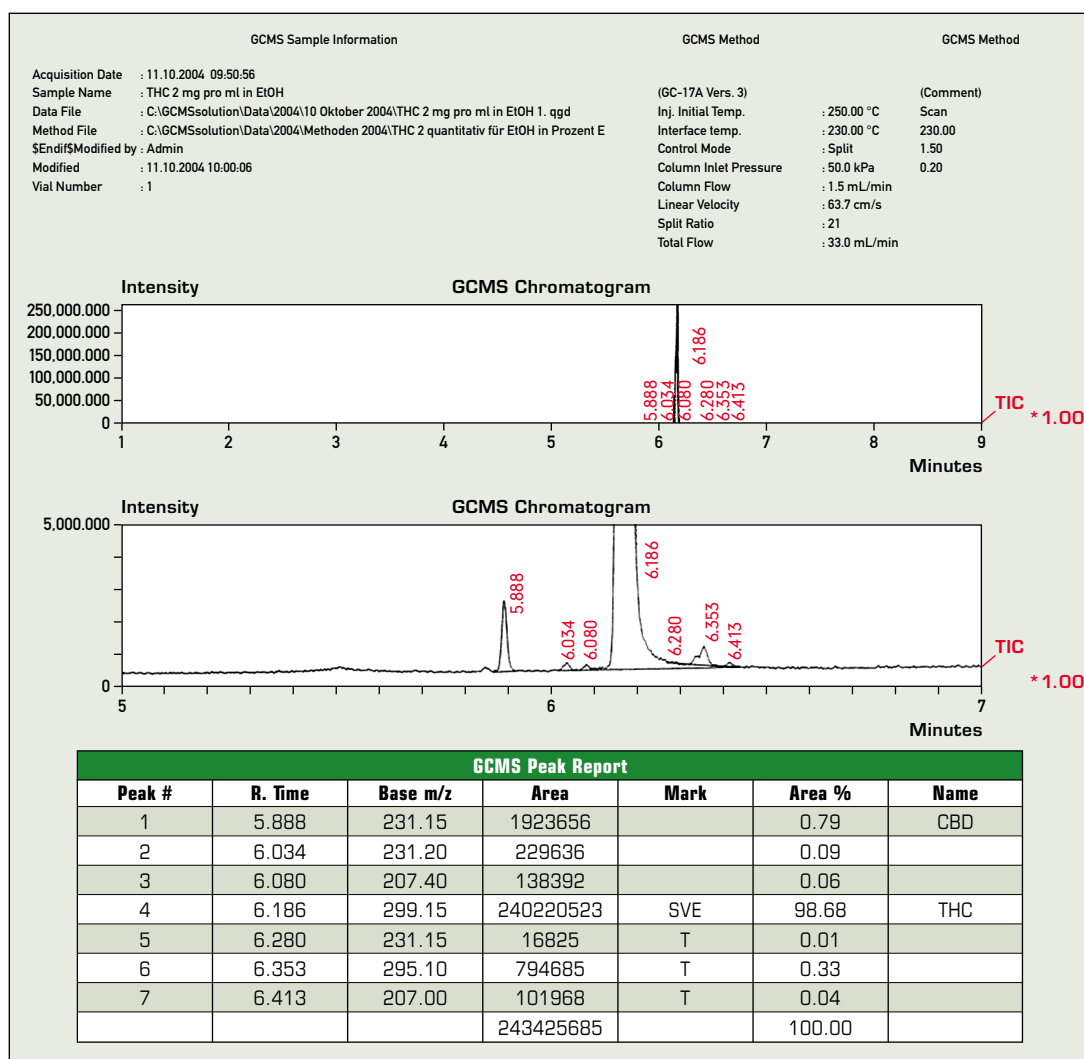


Figure 1: Quality control of dronabinol using the GCMS QP-5000

provide the product for a BTM prescription.

In July 2000, THC Pharm obtained permission under the narcotics law to distribute the active compound dronabinol to pharmacies throughout Germany, as well as Austria and Switzerland. At present, THC Pharm has not only obtained permission to manufacture a standardised cannabis extract but also plans the admission of a cannabis-based drug.

The little interest shown at first by the pharmaceutical industry for cannabis-containing products has changed considerably. In addition to the appearance of copycat products, the re-introduction of cannabis products by THC Pharm and current research results by the Max Planck Institute in Munich, Germany, on the endogenous anandamid system related to cannabis, have brought a completely new active compound class to the attention of medical research. The pharmacological potential of these classes of compounds cannot yet be estimated.

Hemp as food additive

Hemp is gaining popularity not only as a medicinal drug but also as an additive in foods – whether directly as ground hemp nut or as essential hemp oil. Hemp seeds as well as their extracted hemp oils not only have a delicate nutty and somewhat lemony taste, but they are also very healthy. They contain, in addition to vitamins B, B1, E and F, essential linol- and linoleic fatty acids and, being free of glutinates, they are also suitable for the manufacture of foods for people suffering from allergies.

The hemp seed and extracted oils do not contain any THC, but the leaves surrounding the seeds can contain varying amounts of THC. THC can therefore only find its way into foods when the hemp seeds have not been adequately purified.

Although there are no threshold values for THC in foods in Germany, only a recommendation of the BgVV (Bundesinstitut für gesundheitlichen Verbraucherschutz und Veterinärmedizin – Now: Federal Institute of Risk Assessment), hemp oils containing foods must be tested for their THC content. For foods – not including beverages and cooking oils – a value of 0.15 mg/Kg is recommended. By observing

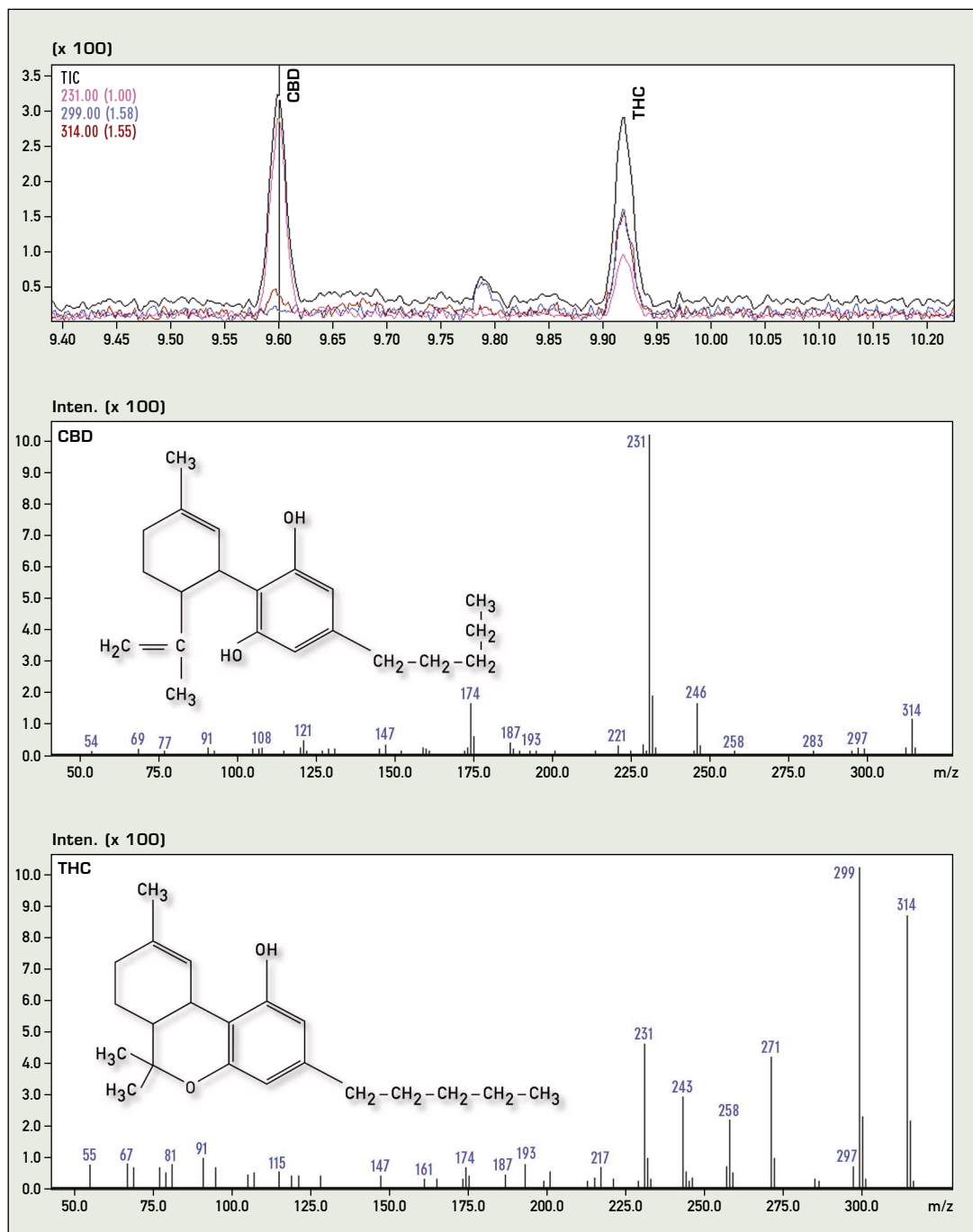


Figure 2: Chromatogram and mass spectra of CBD and THC

these guidelines, no harmful effects can be expected based on current knowledge, and these values serve as an orientation tool for food quality control and analysis in the food industry.

The performance spectrum of THC Pharm also includes the determination of the THC content in foods. For these tests THC Pharm uses Shimadzu's highly sensitive GCMS-QP2010 system. With an internally agreed detection limit of 0.1 mg/Kg (see Figure 2) THC Pharm can measure lower concentrations than the normally specified detection limits of 1 – 2 mg/Kg in food product as well as under the recommended guideline value of the BgVV.

For further information visit www.thc-pharm.de