



# Medical Cannabis

Introduction and Administration Methods



## About STORZ & BICKEL

STORZ & BICKEL is the world's first and leading manufacturer of medically approved Vaporizer for a non-toxic, efficient and validated application of cannabinoids.

The company started more than 20 years ago, when Markus Storz developed the first prototype of today's world-renowned VOLCANO Vaporizer in 1996. The company STORZ & BICKEL was born when Jürgen Bickel became a partner in 2002. Being progressive and having a vision for innovative products in a worldwide growing market are core elements to which the current success of STORZ & BICKEL can be attributed.

STORZ & BICKEL Vaporizers are „Made in Germany“, more precisely „Made in Tuttlingen“, in the 9000 m<sup>2</sup> S&B Vapor Factory. The S&B Vapor Factory is a trend-setting symbol for further potential growth and with its state-of-the-art workstations and open space concept reflects the open company culture both internally and externally.



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## Introduction

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The history of the cannabis plant, one of the oldest cultivated plants in the world, and its flowers goes back millennia. It has long been used by high cultures in Asia, India, Africa, and Central Europe. Until the early 20th century, the plant fibers were used as a valuable raw material for clothing, rope, and other textiles. In the middle of the 20th century, the US initiated a prohibition of the plant, which has since become widely known as an illegal drug.

Because of its therapeutic mode of action, cannabis has recently become the focus of science and media. Countries like Canada, Australia, and Germany recognize cannabis as a medicinal product, and several US states as well as entire countries (e.g., Uruguay) have decriminalized cannabis. Numerous organizations and movements have been set up to promote the legalization of cannabis for medical purposes. Research, science, and medicine are increasingly interested in the mode of action of cannabis, thereby signaling a new era for the cannabis flower and its derivatives.

The effects, hazards, and potentials resulting from the use of the plant can now be better explored in order to shed light on the many open questions from patients and users.

This brochure is intended to help to create a factual basis for an objective and rational discussion of the topic. This condensed overview of cannabis as a medicinal product, its mode of action, and administration methods based on inhalation are intended to facilitate entry into this broad topic.

A vibrant green cannabis leaf with serrated edges is positioned on the left side of the frame. The background consists of horizontal wooden planks with a natural, weathered texture. A semi-transparent dark grey rectangular box is centered horizontally, containing the text "What is Cannabis?".

**What is Cannabis?**



## 1. What is Cannabis?

Cannabis is the Latin term for hemp. Hemp is also known as pot, marijuana, and grass, among other things. These are all names for the same plant. Marijuana is the Mexican slang word for dried cannabis flowers, while hashish refers to the pressed cannabis resin.

Cannabis is a genus of hemp plants and has been cultivated and used as an important crop for many thousands of years throughout the history of mankind. In addition to the drug, the hemp plant also provides fibers for rope, clothing, and paper as well as seeds from which valuable edible oil can be obtained.

The two main types of cannabis are Cannabis Sativa [Fig. 1] and Cannabis Indica [Fig. 2]. In the West, the Sativa species were predominantly used as crops because of their hearty fibers. They are characterized by their high growth. The lateral shoots of the plant are more spacious, and the flowers are comparatively long and narrow. The flowers of Cannabis Indica have a shrub-like appearance. They are shorter and wider and also mature faster.



Fig. 1 - Cannabis Sativa



Fig. 2 - Cannabis Indica

#### Cannabinoids and Terpenes

Cannabinoids are compounds that occur exclusively in the cannabis plant. They can be extracted from the resin of the plant. Currently, about 80 different cannabinoids are known. Based on current knowledge, the  $\Delta^9$ -THC (tetrahydrocannabinol), internationally known as dronabinol [Fig. 3], and CBD (cannabidiol) [Fig. 4] are medically usable.

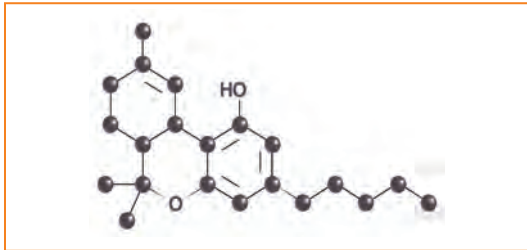


Fig. 3 -  $\Delta^9$ -THC (Tetrahydrocannabinol)

THC is present in the plant as THC acid (THCA) and is primarily found in the female cannabis plant. In this form, the cannabinoid is not psychoactive. Before it can become pharmaceutically active, the THC acid must first be subjected to heat. It is con-

verted into the active  $\Delta^9$ -THC by decarboxylation. The psychoactive effect of cannabis is largely due to the cannabinoid THC. It is now known that it is not only THC (dronabinol) or the THC content that is relevant to the mode of action of cannabis but also the ratio of THC to CBD in the flower.

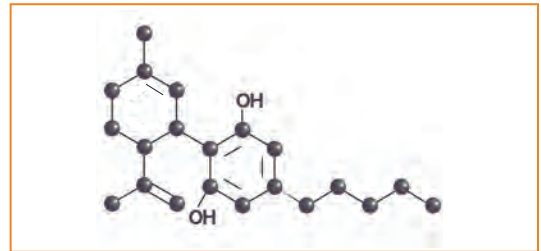


Fig. 4 - CBD (Cannabidiol)

CBD does not have a psychoactive effect but rather an antispasmodic and muscle relaxing effect. Studies have shown that pure THC can cause anxiety, stress, and depression in some patients. Only when THC is administered in combination with CBD is the effect perceived as pleasant by many users.

There are also terpenes in the plant. These compounds are responsible for the fragrance of the cannabis plant. Currently, about 120 different terpenes have been identified in the cannabis plant. Because of the large number of cannabinoids and terpenes in the cannabis plant, an individual interaction takes place for each type of cannabis. This can affect the mode of action.

### The Endocannabinoid System

The discovery of the endocannabinoid system has revolutionized cannabis research. It was not only a great advance in the investigation of the mode of action of cannabis but also fundamentally changed the image of cannabinoids in the minds of many scientists. Until the 1990s, it was still believed that cannabis had a mode of action similar to alcohol and that cannabinoids dissolved in the membranes of the brain cells. However, it is now known that the human body forms similar substances, the endocannabinoids, and has cannabinoid receptors.

The endocannabinoid system consists of cannabinoid receptors, their endogenous ligands, and enzymes for the synthesis of endocannabinoids. This endogenous regulatory system modulates processes such as sleep, appetite, depression, and cognition. One of the main tasks of the endocannabinoid system is neuroprotection. Recent findings have shown that it is also important for the development of cancer as well as bone formation.

To date, two types of cannabinoid receptors have been identified: the CB1 receptor and the CB2 receptor. Both receptors are G-protein-coupled receptors (GPCR). The CB1 receptor is found on many cells throughout the body and also in many organs. However, it is mainly found on neurons, particularly in areas of the cerebellum, the hippocampus, and the cerebral cortex. CB1 receptors account for most of all GPCR receptors in the brain. The CB2 receptor is mainly located on the cells of the immune system.

Endogenous as well as exogenous cannabinoids dock to the CB1/2 receptors, thereby activating them. THC is a partial agonist of the CB1 receptor. In other words, THC activates the CB1 receptors located in the brain. Because CB1 receptors occur more frequently in regions responsible for sensory perception, taking THC intensifies the senses of touch, smell, taste, and hearing. CB1 receptors also have a neuroprotective function in the nervous

system. They inhibit excessively strong signals between nerve cells by inhibiting the hyperfunction of messengers such as glutamate, serotonin, dopamine, and norepinephrine.

The brain stem, which is responsible for the vegetative nervous system and for vital functions such as breathing and the cardiovascular system among other things, shows no presence of CB1 receptors. An overdose of cannabis is therefore not fatal under normal conditions because the vital functions mentioned above remain unaffected by the intake of cannabis.

THC is also an agonist for the CB2 receptor. Because this is located on peripheral tissue in the immune system as well as on white blood cells, it plays a major role in immune functions such as the attenuation of inflammation and allergies (see also 3.1.).

Research in the field is still in its infancy; the endocannabinoid system was only discovered in the early 1990s. However, the findings so far are astonishing and have paved the way for the pharmacological and biomedical research of cannabis.

A person in a white lab coat is writing on a clipboard in the background. In the foreground, there is a white container labeled 'Medical Cannabis' with its lid off, spilling dried cannabis buds onto a wooden surface. A petri dish with a cannabis leaf is also visible.

## Treatment with Cannabis

## 2. Treatment with Cannabis

In countries such as Canada, Italy, the Netherlands, and Israel as well as in many US states, treatment with cannabis has been an option for several years. Other countries like Australia and Germany have recognized the medicinal potential of cannabis in recent times as well.

When administering cannabis for therapeutic purposes, the cannabis flowers and extracts must originate from standardized and controlled cultivation. The treating physician or pharmacist as well as the patients themselves must be able to rely on the content of active ingredients in the medical product. In the case of cannabis flowers, this can be difficult without a standardized process for breeding cannabis flowers because the cannabis plant can be found in different varieties and sizes. The content of THC and CBD differs depending on the plant strain. This can lead to difficulties in the prescription and dosage. In addition, the contamination of the flowers by bacteria, mold, fungicides or pesticides must be ruled out through regular quality controls. Therefore, only cannabis flowers

from a controlled, standardized, and tested cultivation are suitable for a medical application.

There are already some international suppliers of controlled cannabis flowers. For example, Bedrocan BV from the Netherlands has been supplying the European market with medicinal cannabis flowers for several years. The production and quality of these products are supervised by a dedicated cannabis office of the Dutch Ministry of Health.

Another currently important supplier of cannabis flowers for Europe is Canopy Growth Corporation, which sells cannabis flowers according to GMP (Good Manufacturing Practice) and is also licensed under ACMPR (Access to Cannabis for Medical Purposes Regulations). The Pedanios GmbH also imports cannabis flowers from Canada.

#### Indications and Effect

Cannabis and THC have a broad spectrum of effects that can be used therapeutically.  
The most important indications are:

#### Chronic pain

Cannabinoids have been shown to contribute to pain relief; cannabis appears to be particularly effective in treating chronic and neuropathic pain. In contrast, cannabis has little effect on acute pain. Through the administration of cannabis, neuropathic pain in multiple sclerosis, arm plexus damage, pain in rheumatoid arthritis, cancer pain, headache, menstrual pain, chronic inflammation of the lungs, and the like can be alleviated.

#### Spasticity and muscle cramps

In a comprehensive study conducted in 2011, a positive effect of cannabis was demonstrated in 272 out of 572 patients (47.6%) with severe spasticity. Spasticity was reduced by more than 20% in these patients. Also for multiple sclerosis and cross-sectional diseases as well as symptoms such as tremors and ataxia, studies demonstrated positive results when cannabis was administered.



#### **Nausea and vomiting**

Many studies have been conducted on cancer patients to investigate the effects of cannabis on side effects of chemotherapy. Positive results have been noted in the reduction of nausea and vomiting. Cannabis had a similar or stronger effect than the usual antiemetics.

#### **Loss of appetite and emaciation**

Cannabis, especially THC, can have positive effects in cases of loss of appetite and malnutrition. THC is known for its appetizing stimulating effect. In diseases such as anorexia and loss of appetite in HIV patients, weight can be controlled or increased by treatment with THC-rich cannabis.

Other indications with less available data are:  
Tourette's syndrome, attention deficit/hyperactivity disorder (ADHD), posttraumatic stress disorder, itching, behavioral disturbances in Alzheimer's disease, and epilepsy.

#### Risks

Although the positive effect of cannabis is promising in certain indications, as with all medicinal products, the risks and side effects should not be un-

derestimated. Cannabis can have different effects in different patients. Under certain conditions, the risks may be above average.

#### Acute risks and side effects

The psychoactive effect of cannabis (THC) is perceived by many users as pleasant because sensory perception is intensified and a sense of ease is established. In some cases, the psychoactive effect can turn into a dysphoria associated with anxiety and panic. For individuals with a predisposition to psychotic disorders, cannabis can cause or favor psychotic seizures. In patients with heart disease, cannabis should be used with care and

only under medical supervision because cannabis increases the heart rate and can influence the blood pressure.

Other acute side effects may include fatigue, dizziness, and mouth dryness as well as the impairment of memory, cognitive abilities, and sense of time. Normally, tolerance for most acute side effects is built up within a few days.

#### Long-term risks and side effects

Controversial discussions about the long-term effects on cognition and memory in cannabis use are currently taking place. It is assumed that this will only have a negative effect in the case of heavy and long-term cannabis use. Brain injuries such as those which occur with heavy alcohol consumption could not be determined in this context. However, it has been shown that cannabis use can have a negative impact on development during puberty. Therefore, it is recommended that long-term treatment

in patients at the age of puberty be carefully considered. Pregnant or breast-feeding women should also be discouraged from being treated with cannabis.

Furthermore, long-term cannabis use may lead to mild psychological and physical dependency. In the case of a medical treatment with low doses of cannabis, this is very unlikely, although not completely ruled out.



## Administration Methods

### 3. Administration Methods

#### 3.1. Oral Administration

For the administration of cannabinoids there are different administration methods, which primarily depend on the nature of the cannabis preparation. For example, cannabinoids dissolved in oil are only suitable for oral administration.

The cannabis flower is different. It can be consumed as an ingredient (i.e. in baked good or teas) or inhaled. Both methods of administration involve decarboxylation – because the cannabinoids in the plant are present as non-effective acids, the active substances must first be activated by heat (see 1.1.).

#### Oral Administration

Although the use of cannabis infused foods can also have an effect, this is not an optimal medical administration method because for baked goods or tea with cannabis, there are so far no validated recipes to which patients or pharmacies could be directed. In addition, when cannabis is admin-

istered orally, the (self) dosage is made more difficult because the onset of effect can take up to 90 minutes.

In many inexperienced patients, an overdosing cannot be ruled out in the initial administrations because if the effect is not noticed right away, there is a greater probability that the dose will be increased too early.



**The onset of effect can take up to 90 minutes with the oral administration**

#### Inhalation

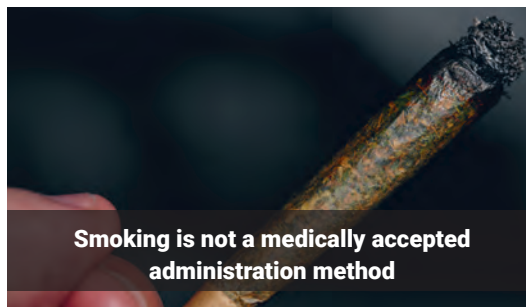
The most popular way to consume cannabis is via inhalation; compared to oral intake, this has a much more rapid onset of effect (within 1–2 minutes). For many patients with acute ailments, this type of administration therefore offers a great advantage over the oral administration. It is also easier for patients to find the right dosage because of the quick onset of effect. If no effect is felt after the first minutes, further inhalations can be taken until the effect is achieved.

There are two possibilities for inhaling cannabis. The most widely used inhalation method is smoking. For most patients, this is the simplest and most convenient method because no special paraphernalia is required. The disadvantage of this method is the toxins that are generated only when the dried flowers are burned.

Toxic combustion substances such as polycyclic aromatic hydrocarbons (PAH's), ammonia, and

carbon monoxide can adversely affect the health of patients. This method is therefore not acceptable for medical use, especially when smoke-free evaporation inhalers are available.

The preferred method is vaporization. This yields short-term effects while minimizing combustion pollutants.



#### The Vaporization Method

For vaporization, cannabis flowers, cannabis extracts, or substances such as THC or CBD are heated in a vaporizer. Cannabinoids generally vaporize at temperatures above 180°C (356°F).

At a temperature of 210°C (410°F), THCA, CBDA, and the terpenes are almost completely dissipated without a combustion taking place.

In the vaporization method, the active ingredients are converted into an aerosol, which is inhaled by patients. The droplets are absorbed by the alveoli and thus enter the blood circulation relatively quick-

ly; the onset of effect takes place after 1–2 minutes. In the case of inhalation, the effect can last for 2–4 hours.

The world's first medically approved Vaporizers for the inhalative application of cannabinoids are the VOLCANO MEDIC 2 [Fig.1] and the MIGHTY+ MEDIC [Fig. 2] from STORZ & BICKEL GmbH. The Vaporizers are developed and manufactured in Tuttingen, Germany.

The VOLCANO has been used in cannabis research for more than 15 years.



Fig. 1 - VOLCANO MEDIC 2



Fig. 2 - MIGHTY+ MEDIC







VAPORMED

Less than 10 years ago, some countries were already well ahead of Germany; at this time, cannabis was already being grown and distributed for medical use in Canada, Israel, and the Netherlands. However, patients were often left alone with the administration. For a lack of alternatives, they smoked the flowers to the detriment of their health. Doctors justify this only if the benefit outweighs the risk.

The demand for a medically acceptable solution for inhaled administration was correspondingly high. For this reason, the two entrepreneurs Markus Storz and Jürgen Bickel developed the world's first medical cannabis vaporizer, the VOLCANO MEDIC. The VOLCANO MEDIC was placed on the market in 2010. It was specially developed for the medical administration of cannabinoids and consists of a Hot Air Generator and a removable Valve Balloon.

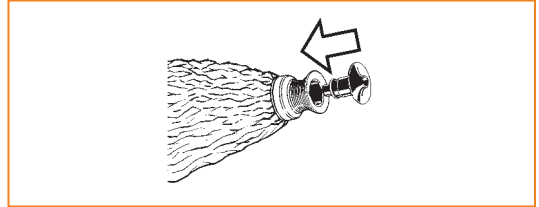
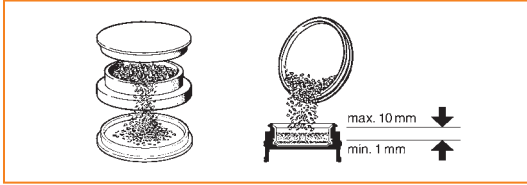
#### VOLCANO MEDIC 2

In 2019 the advanced development of the VOLCANO MEDIC - the VOLCANO MEDIC 2 - was launched. It provides, among other things, a second inhalation method via a tube which can be used for direct inhalation. First, the cannabis flowers are pre-ground by the included Herb Mill to increase the surface area of the material to be vaporized and thus ensure the most efficient administration possible.



## 4. Medical Cannabis Vaporizer

### 4.1. VOLCANO MEDIC 2



The Filling Chamber is then filled with the substance to be vaporized. The filled Chamber is placed on the Hot Air Generator, and the empty Valve Balloon is applied to the Filling Chamber. Air, that is preheated to the set temperature inside the Vaporizer is then pumped through the Filling Chamber with an air pump. The hot air flows through the dried flowers, decarboxylizes the cannabinoid acids, and vaporizes the effective cannabinoids into a respirable aerosol. The aerosol is collected in the Valve Balloon and cooled. The Valve Balloon is removed from the Filling Chamber and fitted with a Mouthpiece. Accordingly, only the cooled and de-electrified Valve Balloon is used. This can also be safely used in bed or even in the bathtub.

#### The Use of Hemp Flowers with the VOLCANO MEDIC 2

If the instructions for VOLCANO MEDIC 2 are followed, the systemic bioavailability of vaporized cannabinoids from hemp flowers in the Valve Balloon is approx. 50% and in the tube approx. 43%. For comparison: The systemic bio-availability of orally absorbed cannabinoids is below 15%.

When using the Valve Balloon and a vaporization temperature of 210°C (410°F), the following reference values for the VOLCANO MEDIC 2 have been validated in studies:

<b>Drug (Filling Chamber content)</b>	<b>Cannabinoid content in Drug</b>	<b>Cannabinoid content in Valve Balloon after Vaporization with 210°C (410°F)</b>	<b>Cannabinoid content in blood stream after inhalation</b>
drug A (100 mg)	THC: approx. 19 mg	approx. 15 mg	approx. 10 mg
drug B (100 mg)	THC: approx. 6 mg	approx. 5 mg	approx. 3 mg
	CBD: approx. 7.5 mg	approx. 6 mg	approx. 4 mg

To obtain a reproducible dose with good efficiency, it is recommended to vaporize small amounts of material (100 mg) in the Filling Chamber at the maximum temperature of 210°C (410°F) in only one Valve Balloon.

When using the Tube Kit and a vaporization temperature of 210°C (410°F), the following validated values for the VOLCANO MEDIC 2 have been validated in studies:

Drug (Filling Chamber content)	Cannabinoid content in Drug	Cannabinoid content in Valve Balloon after Vaporization with 210°C (410°F)	Cannabinoid content in blood stream after inhalation
drug A (100 mg)	THC: approx. 19 mg	approx. 15 mg	approx. 8.25 mg
drug B (100 mg)	THC: approx. 6 mg	approx. 4 mg	approx. 2.75 mg
	CBD: approx. 7.5 mg	approx. 5 mg	approx. 3.4 mg

In order to obtain a reproducible dose with good efficiency, it is recommended to vaporize small filling quantities (100mg) once in the Filling Chamber at the maximum temperature of 210°C (410°F).

## 4. Medical Cannabis Vaporizer

### 4.1. VOLCANO MEDIC 2

#### The Use of Dronabinol dissolved in Alcohol with the VOLCANO MEDIC 2

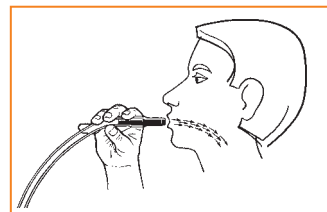
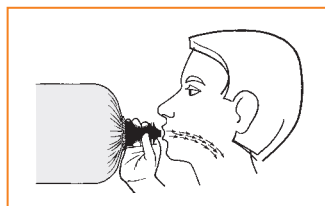
When using dronabinol or cannabis extract (dissolved in alcohol), a Filling Pad made of stainless steel wire mesh is inserted into the Filling Chamber as a carrier. Because the alcohol in the solution is not to be inhaled, a separation can be carried out by vaporizing the alcohol beforehand at temperatures of up to 100°C (212°F). In this temperature range, no cannabinoids vaporize, while the alcohol volatilizes rapidly (in up to 30 sec).

Because alcohol has a characteristic odor, it is easy to determine whether the Filling Chamber is free of alcohol. Dronabinol is odorless and tasteless.

After the alcohol has vaporized, the device is heated to 210°C (410°F). A large digital display with display of the set-point and actual temperature allows the patient to set the temperature.

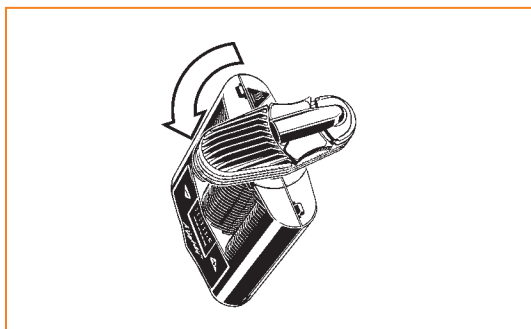


The cannabinoids can then be vaporized from the Filling Pad and inhaled.



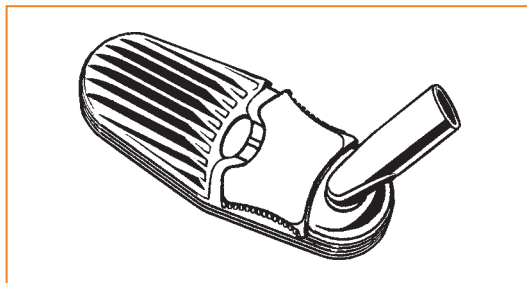
#### MIGHTY+ MEDIC

The MIGHTY+ MEDIC is one of the world's first medically approved portable Vaporizers for cannabinoids. This Vaporizer is a battery-operated handheld device consisting of a Hot Air Generator and a Cooling Unit.



up to the set temperature. The MIGHTY+ MEDIC has a digital display with the set-point, actual temperature, and battery charging display.

After the desired temperature has been reached, it can be inhaled through a Mouthpiece.



As with the VOLCANO MEDIC 2 (4.1), dried and crushed cannabis flowers are also used. These are filled into Dosing Capsules, which are then inserted into the Filling Chamber. The Cooling Unit is then attached, and the Vaporizer is switched on with the push of a button. The Hot Air Generator then heats

### The Use of Hemp Flowers with the MIGHTY+ MEDIC

Studies have shown that approximately 50% of the cannabinoids contained in the hemp flower are found in the aerosol produced by the MIGHTY+ MEDIC. When this aerosol is inhaled, about 65% of

the aerosol enters the blood circulation through the alveoli. The rest is exhaled. The medically effective cannabinoids THC and CBD behave in a similar manner.

At a vaporization temperature of 210°C (410°F), the following values are obtained for hemp flowers with a cannabinoid content of 19% THC and 0% CBD:

Amount of hemp flowers	Cannabinoid content in drug	Cannabinoid content in aerosol	Cannabinoid content in the blood stream after inhalation
50 mg	THC: 9.5 mg	approx. 5 mg	approx. 3 mg
100 mg	THC: 19 mg	approx. 9.5 mg	approx. 6 mg
150 mg	THC: 28.5 mg	approx. 14 mg	approx. 9.5 mg



Values for hemp flowers with a cannabinoid content of 6% THC and 7.5% CBD:

Amount of hemp flowers	Cannabinoid content in drug	Cannabinoid content in aerosol	Cannabinoid content in the blood stream after inhalation
50 mg	THC: 3 mg CBD: approx. 3.2 mg	approx. 1.5 mg approx. 1.6 mg	approx. 1 mg approx. 1.1 mg
100 mg	THC: 6 mg CBD: approx. 7.5 mg	approx. 3 mg approx. ca. 3.7 mg	approx. 2 mg approx. 2.3 mg
150 mg	THC: 9 mg CBD: approx. 11 mg	approx. 4.5 mg approx. 5.5 mg	approx. 3 mg approx. 3.5 mg

In order to reach these values, the patient must inhale until no more aerosol can be seen during exhalation. The contents of the Filling Chamber are then exhausted.

### Important Instructions

The VOLCANO MEDIC 2 and MIGHTY+ MEDIC must not be used if the user suffers from respiratory or lung problems. Depending on the density, the vapors can irritate airways and lungs, which can

## 4. Medical Cannabis Vaporizer

lead to coughing fits. Although the inhalation of vaporized cannabis causes much less irritation than smoking, inexperienced users initially need a habituation period in order to find the optimum temperature for the administration. The user should consciously inhale. Laughter, yawning, and speaking during the administration should be avoided because this can lead to coughing.

### Dosing Capsules (for single Use)

For ease of handling and to make dosage easier for the patient and the physician, Dosing Capsules are available. These can be filled in advance by care staff, family members, or the patients themselves. In this way, administration according to the prescription is facilitated for the patient. The Dosing Capsules can be used both with the VOLCANO MEDIC 2 (the Dosing Capsule has to be inserted into the Dosing Capsule Adapter) and with the MIGHTY+ MEDIC.

When using dronabinol dissolved in alcohol, Dosing Capsules with a Filling Pad are available for the VOLCANO MEDIC 2.



## 4. Medical Cannabis Vaporizer

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The VOLCANO MEDIC 2 and the MIGHTY+ MEDIC provide scientifically validated methods for inhaling cannabinoids. With the MIGHTY+ MEDIC, cannabis flowers of all manufacturers can be used. With the VOLCANO MEDIC 2, cannabis extracts, dronabinol (THC) and CBD from all manufacturers can be used in addition to cannabis flowers provided that the extracts are alcohol-based. When it comes to steeping teas, baking cookies, or smoking flowers, there are no validated recipes and procedures to our knowledge. Numerous scientific studies carried out with the STORZ & BICKEL Vaporizers can be reviewed at [www.vapormed.com](http://www.vapormed.com).

## 5. Further Reading

### Recommended Literature

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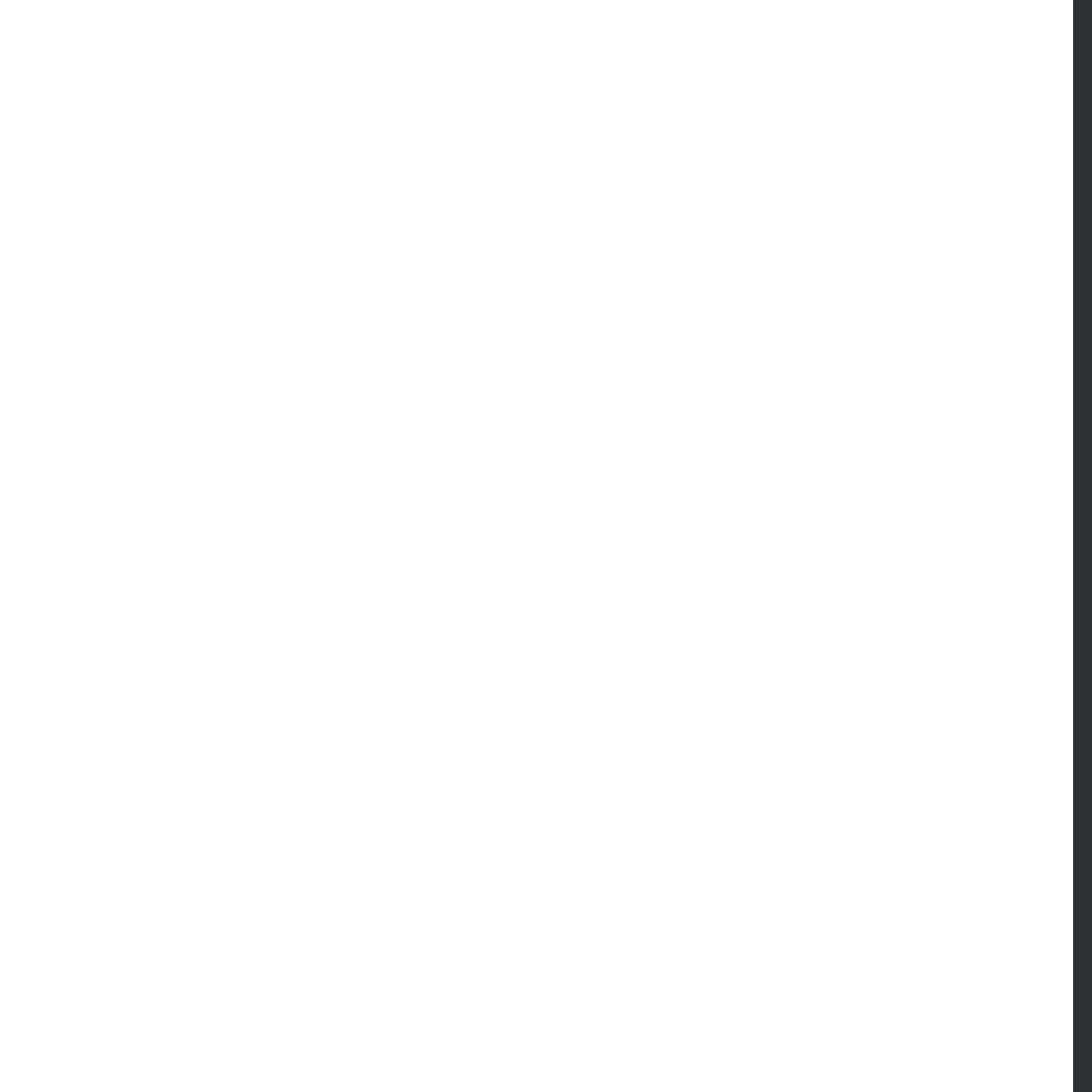
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**Do you have questions?**

We would be happy to assist you personally.



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