IOI OLEOCHEMICAL

PHARMA

CANNABINOID FORMULATIONS

Core Benefits of MCT oil

IOI Oleo GmbH

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According to recent market research, the European market for CBD products intended for medical and recreational use was valued at around €500m in 2018/2019. Estimated growth potential for the European market in the next couple of years is well beyond €1bn. According to current geographic distribution, Europe and the United States are projected to account for roughly 70-75% of global consumption. The growth forecast for Europe's CBD market is 400%[2]. Oils and tinctures rank as the preferred route of consumption, followed by pills and capsules.[2] Additional forms of administration can be semi-solid formulation for topical application through the skin, vape pens, suppositories and oral preparations for companion pets.

For high-end medical applications, CBD and other cannabinoids promise a mild treatment for several neurological and psychological ailments ranging from PTSD and anxiety to MS, epilepsy and chronic pain[3].

IOI's portfolio of lipid excipient specialties connects incredibly well with these delivery routes for cannabinoids and is perfectly suited to address formulation challenges such as solubility and stability.

MIGLYOL® 812 N has shown excellent stability against stress factors and oxidation making it an excellent choice for oil and tincture formulations.

[1] https://cannabusinessplans.eu/european-hemp-market-legalization-and-opportunities/
[2] https://www.healtheuropa.eu/cbd-market-to-grow-400-in-europe/98021/
[3] https://www.rollingstone.com/culture/culture-news/new-study-cbd-market-22-billion-2022-722852/

Selecting the right carrier for oils and tinctures

A variety of carrier oils are utilized for the manufacture of tinctures and oil droplet formulations. Cannabinoid isolates are dissolved in lipid oils to create various product types, ranging from dietary supplements to recreational use and prominently also medicinal registrations. Maximizing shelf life and formulation stability is one of the primary concerns during the development of any new product. Rancimat testing is a well-established method for the determination of oxidation stability in fats, oils and fat-containing preparations.

MIGLYOL® 812 N

- Ph. Eur/ USP "Medium Chain Triglyceride"
- High stability for maximized shelf life
- No need for antioxidants
- Transparent, odor-, smell- and tasteless
- 36 months of shelf life

Rancimat data is used for raw material selection during early product development phases. It is a well-accepted indicator for raw material stability and potential shelf life of finished products, extrapolating the effects of:

- time
- exposure to light and temperature
- oxygen

The effect of these stress factors on the examined samples is monitored by conductivity measurement. Conductivity increases are usually associated with oxidative cascades (autoxidation), which alter the chemical structure of constituents in the examined sample.
The formulated form must remain stable from the time of production, during distribution around the world, on shelves in various climates and finally over repeated opening cycles during product consumption.

Oxygen and Temperature – Stress Factors for Lipids

Table 1 contains the initial and final conductivities measured in samples of hemp oil, sesame oil, olive oil and MIGLYOL® 812 N. Testing conditions were 48 h at 100°C with constant air flow of 19 L/h on a Metrohm 892 Professional Rancimat.

Carrier Oil	Conductivity at t_0 [µS/cm]	Conductivity after 48 h [µS/cm]	Induction time[4] [h]
Hemp Oil	1	1.900	6
Sesame Oil	1	785	15
Olive Oil	1	28	> 47
MIGLYOL® 812 N	1	2	-

Table 1: Initial and final conductivities of examined carrier oils samples under Rancimat testing

Rancimat Curves of Cannabionid tincture carrier oils

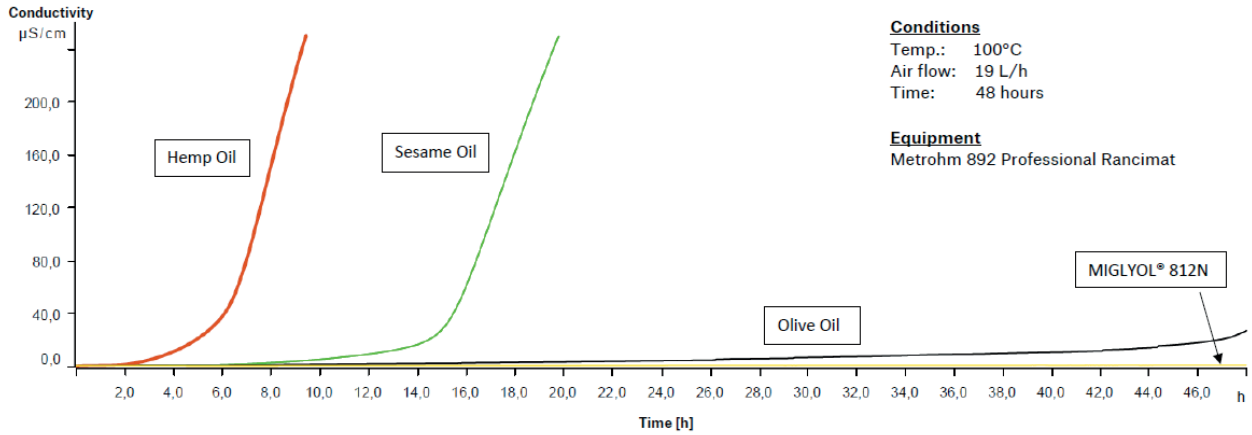


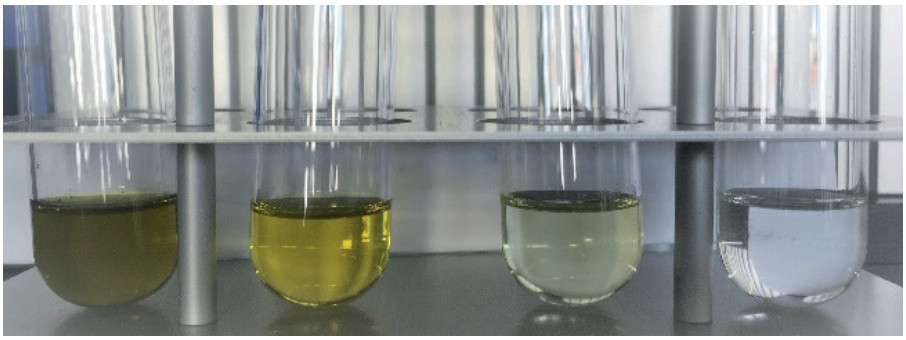
Figure 1: Rancimat curves for Hemp oil, Sesame oil, Olive oil and MIGLYOL® 812N

Plotting the conductivity development in each sample over time as in figure 1 indicates the typical induction time for each sample, when autoxidation accelerates exponentially.

[4] Time span during which autoxidation is relatively slow, before speeding up; corresponding to the flat slope sections of plots in figure 1, with small increases of conductivity.

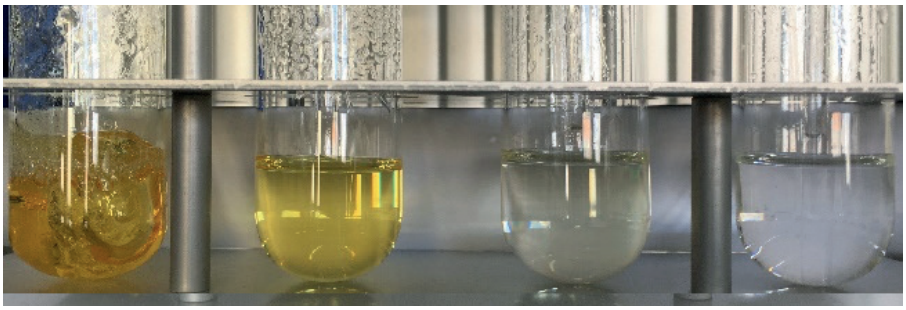
The following pictures show how different oils can be impacted by autoxidation. Typically changes in color, odor, taste and/or viscosity can be found.

These phenomena bare a risk of negatively impacted customer experience during consumption or result in a need for shorter product shelf life.



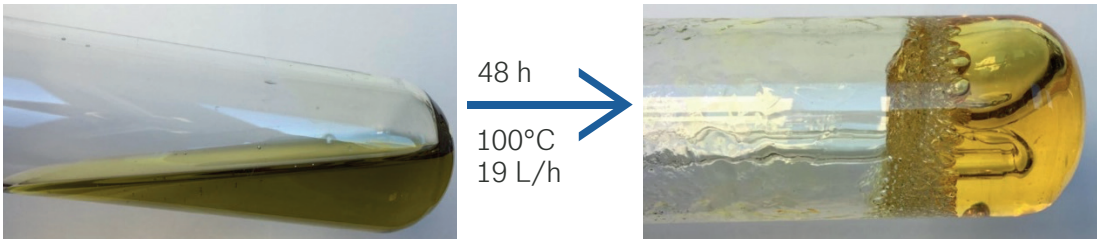
Prestine Hemp Oil, Olive Oil, Sesame Oil and MIGLYOL® 812 N

Rancimat Testing:
48 h
100°C
19 L/h



Hemp, Olive Oil, Sesame Oil and MIGLYOL® 812 N after Rancimat testing

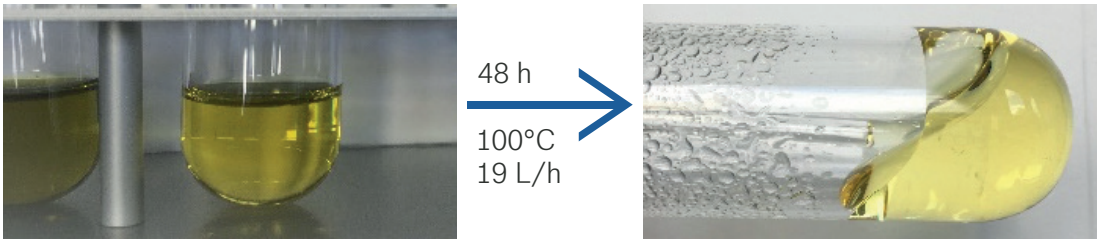
Hemp Oil



Carrier Oil	Conductivity at t_0 [µS/cm]	Conductivity after 48 h [µS/cm]	Induction time[4] [h]
Hemp Oil	**1**	**1.900**	**6**

Hemp oil has experienced a significant change in color and viscosity. The tested sample has shifted from an oily, dark green liquid to a yellow, sticky, highly viscous resin as a result of a polymerization process induced by autoxidation. The final conductivity of the sample was at 1.900 µS/cm.

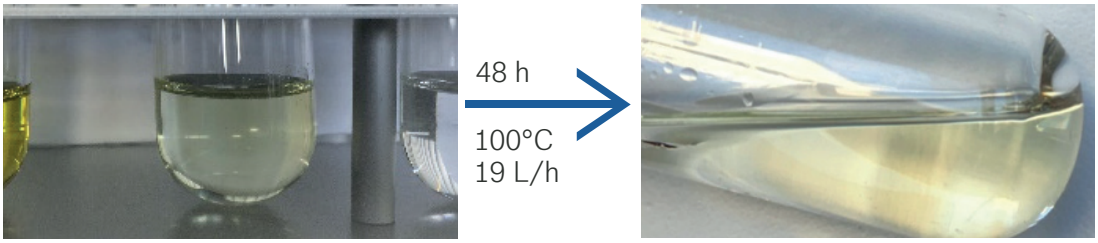
Olive Oil



Carrier Oil	Conductivity at t_0 [µS/cm]	Conductivity after 48 h [µS/cm]	Induction time[4] [h]
Olive Oil	**1**	**28**	**>47**

The color of the olive oil has changed minimally with a slight discoloration. Viscosity of the sample increased and developed an almost honey-like texture. The development of the slope of conductivity increase suggests that the sample was close to reaching its induction time.

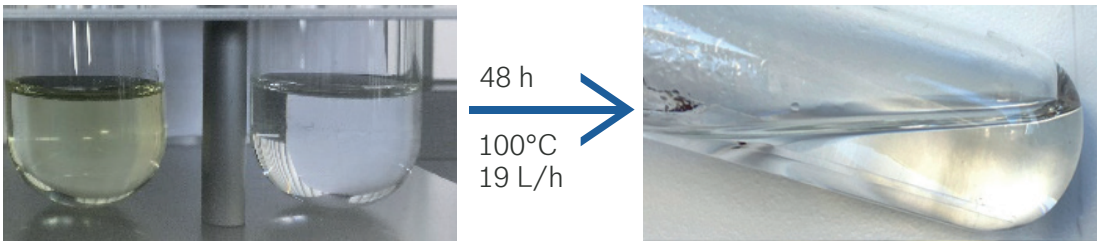
Sesame Oil



Carrier Oil	Conductivity at t_0 [µS/cm]	Conductivity after 48 h [µS/cm]	Induction time[4] [h]
Sesame Oil	1	785	15

Sesame Oil showed minimal discoloration and change in viscosity which might be interpreted as good resistance against ageing. But this oil experienced the second strongest increase in conductivity suggesting a high degree of chemical conversion under testing conditions. Thus rancidity has occured and undesirable odors and flavors can result.

MIGLYOL® 812 N



Carrier Oil	Conductivity at t_0 [µS/cm]	Conductivity after 48 h [µS/cm]	Induction time[4] [h]
MIGLYOL® 812 N	1	2	-

The sample of Miglyol® 812 N has experienced no significant change in color or viscosity. The increase in conductivity was 1 µS/cm.

The natural content of antioxidants in vegetable oils provides some protection against this type of deterioration. The content varies between different crops and harvesting situations and will eventually be exhausted, resulting in a natural threshold for the shelf life of finished products.

MIGLYOL® 812 N - Delivers Quality and Stability

Our excipient MIGLYOL® 812 N is transparent, virtually color-, odor- and tasteless and thus a highly suitable carrier for flavored or unflavored oral droplet preparations.
It is a pure triglyceride lipid oil composed of fully saturated, vegetable ingredients.

The composition, high quality raw materials plus a tightly controlled and validated manufacturing process result in an excipient that contributes excellent stability for finished products with a long shelf life, without the technical need for stabilizers or antioxidants.

- ✓ EU GMP-certified
- ✓ No allergens
- ✓ Pesticide monitoring
- ✓ Excellent color profile
- ✓ RSPO Mass Balance
- ✓ GRAS

As a "de novo" synthesized excipient, MIGLYOL® 812 N is not subject to fluctuations in quality and composition, usually associated with vegetable-based raw materials.

A low impurity profile, high stability against oxidation and liquid over a wide temperature range, MIGLYOL® 812 N supports formulators with all the design space for the development of dosage forms of the highest quality.

MIGLYOL® 812 N is based on natural, sustainable raw materials and can be supplied under the RSPO Mass Balance principle.

This product complies with the requirements of the currently effective Ph. Eur. and USP-NF monographs for "Medium Chain Triglycerides". MIGLYOL® 812 N is generally recognized as safe.

Another aspect of consideration is the caloric profile of medium chain triglycerides (MCTs) as compared to natural fats. Oral consumption leads to metabolization via the portal vein and liver without storage or build up in body tissue. The MCT metabolism creates only small amounts of bile and lipases. Energy is provided as quickly as from glucose with roughly twice the energy density. Metabolites are not deposited in veins and have shown to prevent e.g. arteriosclerosis.

[5] RSPO: Round Table on Sustainable Palm Oil
[6] Mass Balance: Certified palm oil is mixed with conventional palm io but monitored administratively
[7] European Pharmacopeia
[8] Unitd Stated Pharmacopeia - National Formulary

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GET IN TOUCH WITH US!

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