A CBD hybrid with enhanced flexibility

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In 2018, hemp-derived CBD, one of many Cannabinoids present in Cannabis sativa plants, was federally legalised under the US Farm Bill. Although hemp belongs to the same family of plants as marijuana, it contains less than 0.3% THC (delta-9-tetrahydrocannabinol). Unlike THC, hemp-derived CBD lacks any psychoactive effects and does not qualify as a controlled substance. Since its legalisation, CBD has gained massive interest across the regulated medical and pharmaceutical industries, and numerous studies have shown potential benefits of CBD in treating anxiety, depression, sleep disorders, and other related conditions. Several studies have also shown that CBD usage can aid in suppressing inflammatory and neuropathic pain, and several recent publications tested Cannabinoids’ potential for treating inflammatory skin conditions and cutaneous scars. The FDA has recognised the benefits of CBD in its decision to approve the 2019 drug Epidolex®, the first CBD-based oral drug for patients with epilepsy. In addition to scientific industries, there has also been significant interest in CBD in the naturopathic and personal care and wellness markets.

Obstacles and technical background
While CBD may offer a solution to many disorders, its regulation is constantly evolving at global, federal, and state levels. Changes include, but are not limited to, the distribution, use levels, claims, and labelling of Cannabidiol itself, as well as of CBD-containing products. However, regulatory restrictions are not the only obstacles to the use of CBD. There are currently two types of CBD-containing ingredients that can be used in personal care: hemp oil and CBD isolate. Formulating a product containing CBD sounds at first like a relatively easy task, as both hemp oil and CBD isolate are oil soluble. However, hemp oil contains only minuscule amounts of CBD, and the activity of the presented levels is questionable; the hemp oil concentration needed to produce the necessary quantities of CBD may therefore be exceptionally high, thereby ruining the texture and aesthetics of the final product. On the other hand, the use of CBD isolate in personal care products presents its own issues. CBD isolate is both very expensive and very concentrated. To guarantee a homogeneous distribution of the material, it must be properly dissolved in a suitable oil medium before being added to the final product; otherwise it will lack the ability to spread uniformly into a thin layer on the skin. Finally, the solubility parameters of CBD, whether in hemp oil or as a CBD isolate, are limited only to natural oils and hydrocarbons or glycols—preventing its compatibility with silicones and making its use in PDMS (polydimethylsiloxane) restrictive and therefore impractical. Since a substantial portion of both personal care and medical device products consist purely of silicone-based materials such as volatile silicones, silicone fluids, and silicone elastomers, the use of CBD in such products is therefore limited. The full potential of these applications—e.g., soft skin adhesives, scar reduction treatments, and transdermal patches, as well as anti-wrinkle and treatment face masks—is difficult to achieve with pure CBD or CBD isolate.

ABSTRACT
Cannabidiol (CBD) is widely used in the personal care industry and is frequently employed as an additive for moisturisers and topical products. However, CBD can be difficult to incorporate into purely silicone formulations—including volatile silicones, silicone fluids and silicone gels—due its lack of solubility. The rheology and surface energy of CBD also make it difficult to spread into uniform films on the skin. To address these barriers, Gelest has expanded its Vertasil® siloxane modified natural product line to include a new CBD-based derivative. This smart molecule, Vertasil TM-CBD1, specifically addresses formulation obstacles and limitations. As a CBD hybrid fluid, Vertasil TM-CBD1 has an expanded solubility profile that allows the incorporation of CBD into silicone-based products. It also provides lubricity and softness without the greasiness of natural oils. Finally, a distinctive benefit of this new technology is the ability of the CBD derivative to slowly revert back to pure CBD upon release from a silicone matrix.
Trisiloxanyl-cannabidiol hybrid fluid

To fill in this technical gap, Gelest Inc. has introduced a material called Vertasil® TM-CBD1, a multifunctional trisiloxanyl-cannabidiol hybrid fluid. As seen in Figure 1, this CBD derivative contains a trisiloxane group instead of one of the primary hydroxyl sites on the CBD molecule. To achieve this design, CBD isolate was reacted with sodium to form a sodium alkoxide by conversion of a hydroxyl group which in turn was reacted with heptamethyltrisiloxane creating trisiloxanyl substituted-cannabidiol. While other CBD derivatives were considered, this compound was selected due to the fact that it has the maximum amount of natural product that is consistent with the objectives of greater solubility, emollience, and formulation stability.

This patented molecule was specifically designed to extend the solubility parameters and improve the compatibility of Cannabidiol (CBD) with a wide range of materials without compromising the activity or benefits of CBD. Vertasil TM-CBD1 now allows the incorporation of trisiloxane–functionalised cannabidiol isolate into silicone gel matrices such as polydimethylsiloxane (PDMS) and other primarily silicone-based formulations. Additionally, this derivative is compatible with many other cosmetic ingredients, including but not limited to natural oils, hydrocarbons, esters, glycols, silicones, and silicone derivatives. Finally, it also acts as a great solubiliser in formulas combining both silicones and natural oils. The solubility parameters of trisiloxanyl-cannabidiol are summarised in Table 1.

The complete solubility of the CBD hybrid fluid in silicone fluids allows it to be spread into thin films, since the silicone fluids themselves spread to monolayer films. The potential effects of trisiloxanyl-cannabidiol are thus anticipated at concentrations below 0.05%. To demonstrate the improved compatibility of this newly designed material, trisiloxanyl-cannabidiol was incorporated into different PDMS gels to test the performance of the derivative with varying methods.

Trisiloxanyl-cannabidiol loaded into silicone elastomer

First, trisiloxanyl-cannabidiol was absorbed into a high elongation silicone elastomer. A high elongation polydimethylsiloxane elastomer (ExSil® 100) was cut into two equal pieces 1.5 x 2.5 cm and 0.35 g in size and weight, respectively. One piece (sample 1) was placed in a mixed solution of 5 g of trisiloxanyl–cannabidiol and 5 g of propylsiloxane (SiBrid® TM-031). As a control, the second piece (sample 2) was placed in 10 g of hemp seed oil. Elastomers were immersed in their respective solutions for 30 minutes with closed lids to allow the oils to absorb into the elastomers.

After 30 minutes, both samples were removed from solution. Excess solution was gently blotted from the samples using tissue paper, and the resulting silicone pieces were weighed. Sample 1 changed colour from opaque to transparent with an orange tint, weighed 1.41 g (a 400% increase), and swelled to 2 x 3 cm. Sample 2 did not change colour, weight, or size. The visible differences are shown in Figure 2.

These results indicate that lipophilic solutions containing CBD are not compatible with silicone substrates or PDMS gels, as they do not allow for the infusion of CBD into silicone substances, making CBD delivery from the silicone gel elastomer infeasible. Conversely, trisiloxanyl-cannabidiol was able to easily infuse into the silicone elastomer, illustrating its compatibility with the material.

To confirm both the presence of CBD in the silicone gel and release from the gel, thin-layer chromatography (TLC) was performed. The silicone elastomer containing trisiloxanyl-cannabidiol (sample 1) was washed in deionised (DI) water three consecutive times. For each wash, the sample was placed in a vial containing 10 g of DI water and shaken for 10 seconds. The water from each wash was collected and analysed for the presence of CBD. A basic TLC method was used to analyze samples with 20% ethyl acetate in hexanes. CBD isolate was compared to a hydrolysed sample of trisiloxanyl–cannabidiol as well as to each of the washes. When testing the CBD isolate, the TLC plate showed one dark brown spot. The hydrolysed trisiloxanyl–cannabidiol and all three washes also showed spots in the same location, indicating the presence of CBD. These findings are shown in Figure 3.
Trisiloxanyl-cannabidiol loaded in PDMS gel

In a second example, trisiloxanyl-cannabidiol was added to polydimethylsiloxane and cured into the gel. To accomplish this, two parts were prepared. For part A, 21.8 g vinyl-terminated polydimethylsiloxane (Gelest Gel D200A) and 0.8 g fumed silica (CAB-O-SIL M5) were added to a Flacktek® cup and mixed by hand until the silica was incorporated. In a vial, 7.2 g of the D5 replacement propyltrisiloxane (SiBrid® TM-031) and 7.2 g trimethylsilylsilicate resin (Dowsil® MQ 1600) were added together and heated at 80°C until the mixture was homogeneous. Once the mixture cooled, it was added to the Flacktek® cup along with 0.2 g trisiloxanyl-cannabidiol and all components were combined using a Flacktek® mixer. Part B (Gelest Gel D200B) was then added and incorporated using the Flacktek® mixer.

As a control, a PDMS gel containing hemp seed oil was prepared according to a similar process. In lieu of trisiloxanyl-cannabidiol, 2.0 g of Cannabis Sativa seed oil (hemp seed oil) was added to achieve a similar CBD loading level into the gel. Exact formulations for the two gels are summarised in Table 2. Both formulations were poured into individual 2-inch diameter aluminum pans and cured in the oven at 105°C for 80 minutes.

The PDMS gel with trisiloxanyl-cannabidiol cured into a free-standing gel appeared colourless and semi-transparent while the PDMS gel with hemp seed oil presented as yellow, sticky, and soft as shown in Figure 4. After sitting at room temperature for 24 hours, the PDMS gel with hemp seed oil developed a thin oil film on its surface, indicating separation of the hemp oil from the silicone gel. The PDMS gel with trisiloxanyl-cannabidiol showed no separation after 24 hours and remained a free-standing gel. These results demonstrate the more successful and facile incorporation of trisiloxanyl-cannabidiol into silicone formulations compared to alternative CBD-containing oils such as hemp seed oil.

Release of CBD from silicone gel

The trisiloxanyl ‘tipped’ tail of the CBD derivative promotes favourable interactions with silicone substrates. Trisiloxanyl-cannabidiol can be absorbed into a silicon substrate in a homogeneous fashion while maintaining optical clarity and stability with no phase separation. Exposure of the silicon substrate loaded with the trisiloxane-cannabidiol to water results in hydrolysis at the silicon-oxygen-carbon linkage, releasing and reforming the original, fully active CBD molecule at the interface. The release mechanism is illustrated in Figure 5. This system has potential application use for the controlled release of CBD from silicone materials and future work will be focused on analysing the rates of controlled CBD release as well as interaction at the substrate-skin interface.

Conclusion

CBD is used extensively in the personal care industry for a wide variety of applications. However, due to its inability to spread uniformly into a thin layer on the skin without further dilution in a suitable oil medium, pure CBD can be difficult to use when formulating products. Many CBD-containing products, such as hemp oil, contain only small amounts of CBD, and thus require large use levels in formulations to achieve appropriate CBD activity. Additionally, neither CBD isolate nor CBD-containing products are soluble in silicone oils or compatible with silicone materials. Since silicone materials are used extensively in personal care applications, there is an entire market segment currently unable to effectively use CBD in its products.

Vertasil TM-CBD1 (trisiloxanyl-cannabidiol) is a material specifically designed to address the current limitations on CBD use in personal care applications, with an expanded solubility profile to silicone oils and easy integration into silicone gels. This new product is anticipated to enable many applications, including soft skin adhesives, scar reduction treatments, transdermal patches, and anti-wrinkle face masks. Furthermore, Vertasil TM-CBD1 is easily incorporated by creating a thin emollient film and provides lubricity and softness without the greasiness of natural oils. Vertasil TM-CBD1 also has the potential to be used for controlled CBD release. Since this material is a CBD derivative, it may rely on a different set of federal and state regulations than CBD itself, which may be important for interstate transport, claims, and labelling. Vertasil TM-CBD1 is a unique, unmatched material that will expand the use of CBD in the personal care industry.

References


![Figure 2](image-url)

**Figure 2:** Vials on the left contain trisiloxanyl-cannabidiol (orange); vials on the right contain hemp oil (green). A) Two pieces of silicone elastomer before submersion in trisiloxanyl-cannabidiol and hemp oil, respectively. B) Silicone pieces placed in oils and left with closed lids at time = 0 minutes. C) Silicone pieces after removal from oil: the silicon piece placed in trisiloxanyl-cannabidiol has swollen and taken on a visibly orange tint, indicating absorption of the oil, the silicon piece placed in hemp oil shows no change, indicating no oil absorption.

![Figure 3](image-url)

**Figure 3:** TLC plate showing the presence of CBD in hydrolyzed trisiloxanyl-cannabidiol and in the three washes from the gel.

**Table 2: Formulations of PDMS Gels Containing Hemp Seed Oil and Trisiloxonyl-Cannabidiol**

<table>
<thead>
<tr>
<th>Ingredients</th>
<th>Trade Name</th>
<th>Hemp</th>
<th>TM-CBD1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Part A - Polydimethylsilicone Gel</td>
<td>Gelest Gel D200A</td>
<td>50.00</td>
<td>54.50</td>
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<tr>
<td>Propyltrisiloxane</td>
<td>SiBrid TM-031</td>
<td>18.00</td>
<td>18.00</td>
</tr>
<tr>
<td>Trimethylsilylsilicate resin</td>
<td>Dowsil MQ 1600</td>
<td>18.00</td>
<td>18.00</td>
</tr>
<tr>
<td>Fumed Silica</td>
<td>CAB-O-SIL M5</td>
<td>2.00</td>
<td>2.00</td>
</tr>
<tr>
<td>Cannabis Sativa Seed Oil</td>
<td>Hemp Seed Oil</td>
<td>5.00</td>
<td>0.00</td>
</tr>
<tr>
<td>Trisiloxanyl-Cannabidiol</td>
<td>Vertasil TM-CBD1</td>
<td>0.00</td>
<td>0.50</td>
</tr>
<tr>
<td>Part B - Polydimethylsilicone Gel</td>
<td>Gelest Gel D200B</td>
<td>7.00</td>
<td>7.00</td>
</tr>
</tbody>
</table>
Figure 4: Release mechanism of trisiloxanyl-cannabidiol interacting with silicone gel. Upon introduction of water, the Si-O-C bond is hydrolyzed, resulting in the formation of fully active CBD.

Figure 5: Left: PDMS gel cured with hemp seed oil. Right: PDMS gel cured with trisiloxanyl-cannabidiol.

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