HEMPE's CBD-Infused Gels Measurably Improve Users Quality of Life and Significantly Helps Reduce Aches and Strains, Aligning or Exceeding with Expectations from the Clinical Literature

Professor Milyan Hills - Head of Scientific Writing, Healthcare International Research Limited.

Introduction

The purpose of this White Paper is to compare findings from a recent piece of research undertaken with users of HEMPE's CBD-infused gels against reports from the clinical literature on large scale studies testing similar gels on athletes and others.

The Paper begins by establishing the mechanisms by which CBD-infused gels work and a summary of key historical and contemporary scientific understandings of the Endo-Canniboid System (ECS) in the human body. The Paper then presents insights from current medical literature on the proven efficacy of topically applied CBD-infused products. These insights detail significant improvement in perception of aches and strains, as well as an enhanced quality of life. Next, recent research with users of HIR's HEMPE CBD-infused gels is compared and contrasted with this literature.

Finally, the Paper discusses the findings and demonstrates strong alignment between expectations from the published literature and user-reported experience of HEMPE's CBD-infused gels. A short observation is provided for the need for a large-scale clinical trial – which HEMPE's parent company HIR will be taking forward in the following months.

HEMPE's Scientific Heritage: Built on a Historical Record of Folk Medicine Use of Cannabis

HEMPE and HIR have a unique scientific heritage: the Czech Republic's leading

contribution to the medical and therapeutic understanding of active ingredients in the hemp (cannabis) family of plants. We use our archive of research undertaken by the groundbreaking Czech scientist Professor Jan Kabelik of the Research Institute of Medicinal Plants, Velké Losiny. HIR taps into over 60 years of excellence in scientific research and formulation of CBD-infused products.

Professor Kabelik arguably re-discovered the curative powers of cannabis plant extract and it is perhaps no surprise that a Czech scientist would do so for, as he noted, Czechs have been in the vanguard of the therapeutic uses of the cannabis plant: "the ancient Czechs were familiar with cannabis porridge. Medieval monasteries used a large amount of seed for soups and porridges" (Kabelík: 1954).

Kabelík conducted extensive research in the literatures of herbaria and the classics, and was able to remind us of even more historic scientific knowledge relating to the topical use of what we now know as CBD-infused products. For example, Galen (b. 129ce - d. c216) and Dioscorides (b. around AD40, died around AD90).) and apparently "both of them knew the analgesic, forgotten by today's medicine, properties of hemp stems. Juice from it dripped into the ears for pain" (Kabelík: 1954).

He continues: "Tabernaemontanus [b. c1525 – d. c1590] and Kramerarius [medieval times, specific dates unclear] advise to apply fresh cannabis leaves to burns and not to let them dry out, and even better: pound the cannabis in a mortar and make an ointment with butter (we know today that butter has effects similar to azulene, anti-inflammatory)" (Kabelík: 1954). We now also understand that fats help with the skin's absorption of CBD-infused ingredients.

Why does applying CBD-infused gel to the skin reduce aches and pains?

Just as aspirin was originally produced from concentrated willow tree bark (and ibuprofen can be made from pine trees), CBD is found in plant extracts. All of these compounds work with the body's pathways and systems to reduce aches and pains, target inflammation and support recovery

2

CBD-infused gels target our Endo-Canniboid System (ECS). These compounds interact with the body's 'signaling' of aches and strains that the ECS can reduce. In other words, the Endo-Canniboid System is a resource ready to be used to help us alleviate the limiting effects of post-exercise or sprain aches and strains enabling us to achieve more in the enjoyment of our daily lives and return to working-out sooner.

Contemporary Scientific Descriptions of Canniboid Mechanisms

Empirical research has determined that clinical endocannabinoid deficiency can be inextricably linked to various conditions including pain, inflammatory and neurological conditions (Russo 2004). Thus, if the human body fails to produce enough endocannabinoids, then supplementation of exogenous plant-based cannabinoids may be needed. Clinical studies have shown altered endocannabinoid signaling in patients with chronic pain and additional pioneering research has demonstrated that either Delta-9-tetrahydrocannabinoid (THC) or Cannabidiol (CBD) can be an effective therapeutic option for patients with neuropathic pain and other types of chronic pain (Lynch and Campbell 2011).

CBD oil has been found to achieve significant improvement in pain and other disturbing sensations in patients with peripheral neuropathy (Xu et al. 2020). Additional studies conclude that the topical application of CBD is linked to pain relief and inflammation reduction. One study indicates that CBD oil can have a significant effect on delayed onset muscle soreness from exercise induced muscle damage (Hatchett et al. 2020). A second study on professional rugby players found that the efficacy of CBD does help alleviate pain, enhance recovery, and promote sleep (Kasper et al. 2020). A third study found that CBD has potent anti-inflammatory effects on the body and can stop inflammatory responses by interacting with cannabinoid receptors located in the immune cells (Ashton 2020).

CBD is a non-psychoactive molecule extracted from the hemp (or its cousin the cannabis) plant, which interacts with (or modulates) the CB1 and CB2 cannabinoid receptors in the central nervous system. As a recent publication by Masquetti et al. states:

3

Many other non-CB1 and CB2 mechanisms have been proposed to explain the therapeutic effects of CBD [...]. Due to these mechanisms of action, CBD can be used as an anti-aging, anti-inflammatory, antioxidant, and for pain relief for topical applications, for multiple sclerosis and neuropathic pain (Masquetti et al. 2024).

Grinspoon, writing as a doctor and from a senior position at Harvard University's health

publishing division, recently noted that:

human studies are substantiating the claims that CBD helps control pain. One animal study from the European Journal of Pain suggests CBD could help lower pain and inflammation due to arthritis when applied to skin. Other research identifies how *CBD may inhibit inflammatory and neuropathic pain, which are difficult to treat* (Grinspoon 2024, emphasis added).

HEMPE's User Research: Background

Healthcare International Research has completed a major piece of research with users of its 'HEMPE' CBD-infused gel products. The following sections demonstrate that its reported impact on aches and strains matches or exceeds clinical trial evidence from the peer-reviewed literature.

Over a period from June 2023-September 2024, verified purchasers of HEMPE opted, with no inducement, to share their experiences in using CBD-infused gel. Adhering to conventional ethical standards and procedures, the survey platform 'SurveyMonkey' was used to collect and analyse findings. Carefully designed, 12 questions sought to gather both quantitative and qualitative data about user experience. For qualitative data, free text fields enabled respondents to add in anything that they wished to state.

For quantitative data, the survey largely adopted an established uses of the Likert scale to report both baseline perceptions of aches and strains as well as changes after 3 days and 3 weeks ('on a scale of 0 to 10' where 0 was the absence of pain For example).

The survey attracted 135 responses. We have cited the words used in qualitative responses verbatim, rather than employing paraphrasing used in some other studies (e.g. Stacy et al. 2021) as we regard it as important to foreground the lived experience of our highly articulate respondents.

Speed of Relief

The survey found that after just 3 days of use, 54% of patients reported an improvement in soreness levels of 50% or more. After 3 weeks, there was an average decrease of more than 53.4% in perceived discomfort, aches or strains. These numbers came as somewhat of a surprise to the research team – they were aware of strong individual anecdotal evidence, but to see this impact reported by a large sample of users significantly exceeded expectations.

Importantly, this finding is supported by patient-reported experience in a recent and significant clinical trial. Even though this trial combined the use of a topical CBD cream with physiotherapy, the reduction reported in pain of 59% is clearly in line with HEMPE gel users experience (Martínez et. Al., 2024).

CBD-gel Improvements Drive Virtuous Benefits

Analysis of the HEMPE user survey also finds that many users were able to do more in the way of movement / exercise as a result of applying the CBD-infused gel, which could be seen as a self-directed form of physiotherapy. It is not unusual for users to have developed their own treatment protocols including CBD-infused gel. Typical, for example, is this report: "Cbd gel gives relief, swimming and light exercise, use of a hot water bottle gives relief". Another athletic user stated: "every time I have any type of muscle injury with training I use hemp twice a day and it allows me to still train without pain". Another user reported, for example: "It allowed me to carry on running and after 3 weeks my knee was fully healed". Another stated: "It allows me to have better mobility".

HEMPE users tended to report immediate relief from symptoms. At the beginning of their use of HEMPE –CBD gel, those with moderate to higher levels of pain (>6), reported a reduction in pain after 3 days of 53% - and after 3 weeks by 55%. Others – unprompted - reported a much more immediate benefit: "Hempe allows me to train even when I'm carrying a little niggle. It gets to work straight away and within 30 mins my pain is manageable enough for me to crack on with training".

Even those with more problematic symptoms experienced benefit. One user, for example, stated benefiting from both increased "mobility and far more manageable pain levels".

These findings align strongly with expectations based on the findings of a clinical study into CBD cream treatment for chemotherapy-induced neuropathy. Baseline pain reported by a patient at 7-10 / 10 decreasing to 4-5 / 10 [a 2-3 point decrease] was mirrored by an average decrease of 3 points reported by HEMPE users (Stacy et al. 2021). It is worth remembering once again that these forms of pain are described by clinicians as: "difficult to treat" (Grinspoon 2024).

Stronger Impact Over Time for More Severe Symptoms

For more extreme pain (>8), the results for HEMPE gel were respectively a 50% reduction in reported pain after 3 days and 59% after 3 weeks. These findings align with a major clinical trial with elite athletes that reported longer-term use of topical CBD had greater benefits as further exercise is enabled (Hall et al. 2023).

Improvement in Quality of Life

HEMPE users report a strong level of improvement in quality of life which is also broadly in line with expectations from the Martinez et al. clinical trial. That found 88.89% of patients reporting an improvement in quality of life versus HEMPE CBD-infused gel users reporting that 90.4% experienced an improvement in quality of life (Martínez et al. 2024). Typical qualitative responses, with original emphasis included, would be: "I'm able to do more without pain. More active. Better sleep too." or "HEMPE HAS CHANGED MY LIFE"

Conclusion

HEMPE users have surprised us with their reporting of the speed and impact of the benefits they feel are gained from our CBD-infused gels. The alignment with findings of clinical trials and studies is striking. We are now actively exploring further research strategies, which we expect will include large-scale clinical studies with both professional sports teams and highly competitive amateur teams. With wider awareness in the scientific, sporting, performance and other communities that there are no psychotropic ingredients in CBD-infused gels produced by highly regulated companies such as HEMPE HELPS, and therefore the risk of reputational and other peril is removed, we look forward to reporting on still more impressive findings.

References

- Ashton, L., CBD and Sports: How hemp oil improve athletic performance, <u>The Center for</u> <u>Advancing Health</u>, (2020) <u>https://cfah.org/cbd-for-athletes</u>
- Grinspoon, P., (MD), Cannabidiol (CBD): What we know and what we don't, <u>Harvard Health</u> <u>Publishing</u> (April 4, 2024) <u>https://www.health.harvard.edu/blog/cannabidiol-cbd-what-we-know-and-what-we-dont-2018082414476</u>
- Hall, N., James, B., Bhuiyan, M.A.N. et al. **Topical cannabidiol is well tolerated in individuals with a history of elite physical performance and chronic lower extremity pain**. J Cannabis Res 5, 11 (2023) <u>https://doi.org/10.1186/s42238-023-00179-8</u>
- Hatchett, A., Armstrong, K., Hughes, B., & Parr, B., **The influence of cannabidiol on delayed onset of muscle soreness**, <u>International Journal of Physical Education</u>, Sports and Health, <u>7(5)</u>, 89-94 (2020).
- Lynch, M.E. & Campbell, F., Cannabinoids for treatment of chronic non-cancer pain; a systematic review of randomized trials', <u>British Journal of Clinical Pharmacology</u>, 72(5), pp.735-744 (2011).
- Kasper, A. M., Sparks, S. A., Hooks, M., Skeer, M., Webb, B. & Nia, H. High prevalence of cannabidiol use within male professional rugby union and league players: A quest for pain relief and enhanced recovery, <u>International Journal of Sport Nutrition and Exercise Metabolism</u>, 30(5), PP.315-322. (2020).
- Martínez, Francisco Martínez; Cabo-Pastor, Marta Belén; Carlos-Villafranca, Félix De; García-Carrillo, Nuria; Jindal, Vidushi; Calvo-Guirado, José Luis., Clinical Study of Analgesic and Anti-inflammatory Properties of Cannabis Derivatives in Patients with Temporomandibular Joint Pathology: Preliminary Study, Indian Journal of Dental Sciences 16(2):p 80-87, (2024).
- Ana Laura Masquetti Fava, Cinthia Madeira de Souza, Érica Mendes dos Santos, Luiza Aparecida Luna Silvério, Janaína Artem Ataide[,] Ana Cláudia Paiva-Santos, Jose Luiz Costa, Daniela Oliveira de Melo and Priscila Gava Mazzola, Evidence of Cannabidiol Effectiveness Associated or Not with Tetrahydrocannabinol in Topical Administration: A Scope Review (Pharmaceuticals, 17(6), 748 (2024).
- Russo, EB., Clinical endocannabinoid deficiency (CECD): can this concept explain therapeutic benefits of cannabis in migraine, fibromyalgia, irritable bowel syndrome and other treatment-resistant conditions?, <u>Neuro Endocrinology Letters</u>, 25(1-2), 31-39 (2004).
- Stacy D'Andre; McAllister, Sean; Jasdeepa Nagi; Giridhar, Karthik V; Ruiz-Macias, Eduardo; et al., **Topical Cannabinoids for Treating Chemotherapy-Induced Neuropathy: A Case Series**, <u>Integrative Cancer Therapies; Vol. 20</u>, (2021).
- Xu, D.H., Cullen, B.D., Tang, M. & Fang, Y., **The Effectiveness of Topical Cannabidiol Oil in Symptomatic Relief of Peripheral Neuropathy of the Lower Extremities**, <u>Current</u> <u>Pharmaceutical Biotechnology</u>, 21(5), pp.390-402 (2020).