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Case Study : Oral Liposomal Beta-Caryophyllene as Adjunct Treatment for Treatment-Refractory Phantom Limb Pain

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Abstract

Post-amputation phantom limb pain (PLP) is a complex neuropathic pain condition affecting up to 80% of amputees, characterized by burning, electric, or shooting sensations perceived in the missing limb. Current pharmacological treatments offer limited efficacy with significant adverse effects. This case report documents a 64-year-old male amputee with 42-year history of post-traumatic PLP who achieved substantial and sustained pain relief using a liposomal β-caryophyllene (BCP) product as an adjunct to his usual high tetrahydrocannabinol (THC) cannabis which was no longer providing pain relief. BCP is a natural sesquiterpene found in several different plants including clove and cannabis and is a selective cannabinoid receptor 2 agonist. The patient demonstrated progressive improvement over two years, with pain severity reduced substantially enabling return to normal functional and social activities. The therapeutic effects of BCP on neuropathic pain and PLP involves actions at the dorsal root ganglion and reduction of inflammation. BCP may synergize with major cannabinoids found in cannabis, including THC and cannabidiol (CBD). This case study suggests that BCP has potential as a novel therapeutic approach for refractory post-amputation pain syndromes, in conjunction with medicinal cannabis. Further research into BCP with and without cannabis in PLP is warranted.

Introduction

Phantom limb pain (PLP) is pain perceived by the region of the body no longer present, and represents a significant clinical challenge affecting amputees worldwide. PLP occurs in an estimated 50-80% of amputees (Richardson & Kulkarni, 2017); global prevalence is estimated at 64% (Limakatso et al., 2020). In 2019 the prevalence of limb loss in the US was 2.3 million (Rivera et al., 2024). In the US in 2019, 564,893 amputation procedures were performed, with the key causes being diabetes and vascular diseases (94%), followed by trauma (6%), cancer (0.2%), and congenital abnormalities (0.1%). Lower extremity amputations comprised the vast majority (~91%) of amputations largely due to diabetes and vascular diseases (Rivera et al., 2024).

The pathomechanisms of PLP are poorly understood and it is difficult to treat (Subedi & Grossberg, 2011). Onset of PLP can be immediate or years after the amputation (Subedi & Grossberg, 2011). Anxiety, depression, stress and other emotional triggers may contribute to the persistence or exacerbation of PLP (Subedi & Grossberg, 2011). There are several different theories including peripheral, central neural and psychogenic mechanisms, however none of these independently explain the phenomenon of PLP (Subedi & Grossberg, 2011).

PLP is often classified as neuropathic pain, though as Richardson and Kulkarini note, there have been no neuropathic pain drug trials with a sufficient number of PLP sufferers to have confidence that they are effective in managing PLP (Richardson & Kulkarni, 2017). Treatment approaches include pharmacotherapy (opioids, tricyclic antidepressants, anticonvulsants and others), surgical intervention, and adjuvant therapies including cognitive behavioural therapy, biofeedback, mirror therapy, transcutaneous nerve stimulation, physiotherapy and others (Subedi & Grossberg, 2011). A review of 38 different therapies for PLP found that overall, quality of evidence was low and concluded that decisions for first-line management of PLP could not be made as the level of evidence is too low (Richardson & Kulkarni, 2017).

This case study describes a 64 year old Australian amputee with PLP who had tried several different treatment approaches including conventional pharmacotherapy and medicinal cannabis for over 40 years. After medicinal cannabis (MC) had stopped working for him, he was treated with a product based on β-caryophyllene, a natural sesquiterpene component of various spices and plant essential oils, which he used in addition to his usual MC.

Case Study

At the end of 2023, a 64-year-old Australian male was referred for a telehealth consultation complaining of PLP which has been occurring since age 21. He had been involved in a motorbike accident where he sustained multiple compound fractures with severe degloving injury, requiring 18 surgical interventions over six months of hospitalization. Despite attempts to salvage the foot through debridement and revascularization procedures, persistent methicillin-resistant Staphylococcus aureus infection necessitated amputation of the foot and partial lower leg.

For approximately 25 years following amputation, phantom pain episodes were episodic and brief (seconds to minutes in duration), occurring infrequently. However, approximately 10 years prior to his initial consultation with PB, pain frequency had increased to roughly once per week with high intensity. Then, starting in 2022-2023, the pain became persistently present, occurring multiple times hourly throughout each day and night. Pain intensity reached 9/10 on a 0-10 pain scale, manifesting as burning and stabbing sensations predominantly in the absent middle three toes of the left foot, occasionally radiating to heel and medial foot regions. In his missing big toe and ball of foot the pain was described as incredibly intense. Pain episodes occurred without warning, lasting from seconds to several hours, with unpredictable onset making sleep impossible and causing significant occupational disruption. The patient reported screaming involuntarily during severe episodes while at work in professional settings. At the peak of pain severity, the patient experienced suicidal ideation secondary to acute psychological distress and a perceived inability to manage symptoms. Sleep was very disrupted because of the pain. He had deep sensitivity along the left anterior stump with manipulation reproducing phantom pain in the missing toes, suggestive of neuroma development. Due to the severity of the pain and disruption it caused to his life, the patient reluctantly retired from work in an office in August 2023.

Prior Treatment

Prior treatments included gabapentin at standard therapeutic doses which was ineffective. He had tried opioids for 10-15 years prior to his consultation and found that he required escalating doses to manage accelerating pain frequency. He ultimately abandoned opioid use due to concerns about dependency risk.

Current Medications

At the time of the first consultation, the patient was taking a daily tablet of proton pump inhibitor for gastroesophageal reflux disorder unrelated to his pain condition.

He was also currently using MC (smoking cannabis flower combined with tobacco) and had been smoking cannabis for several years for pain relief. The patient reported that in the past, smoking cannabis had reduced the pain, providing modest reduction in lower-grade background pain though it had failed to address high-intensity episodic pain. However for several months prior to his consultation with Philip Blair, MD (PB), he reported that the MC was no longer effective for any significant pain relief. He then sought a consultation to explore other options.

Initial Treatment

The patient initiated treatment with BCPlus (liposomal BCP formulation for sublingual/oral administration, manufacturer Cellg8® Wellington, Colorado) administered sublingually at approximately 1-2 milliliters taken under the tongue, retained for one minute with saliva, then swallowed. Initial treatment protocol consisted of regular dosing every 4-6 hours as per physician instructions.

BCPlus contains the following ingredients:

- Active Ingredient Beta-Caryophyllene (BCP) from clove
- Inactive Ingredients: Purified water, Natural flavors, Non-GMO sunflower lecithin, glycerin, stevia leaf extract (as glucosylsteviosides), potassium sorbate (preservative)

He continued to smoke cannabis combined with tobacco, consuming 6-12 joints per day, as he had been doing for many years.

Follow-Up

Within the first two weeks of use of BCPlus as an adjunct to MC therapy, pain severity progressively decreased, becoming less frequent and less intense. After this initial titration period, the patient transitioned to as-needed prophylactic dosing, taking the BCP formulation when pain episodes initiated, while continuing his MC routine.

Over the next few months following the initial consultation, the patient found that optimal pain control was achieved with approximately 2 milliliters of BCP taken sublingually during acute pain episodes or as a prophylactic dose 2-3 hours before anticipated triggering situations (such as long-distance travel). He found that the peak therapeutic effect occurred approximately 60-90 minutes following administration, with pain relief persisting for extended times between doses in many instances. He continued to smoke cannabis daily as he had previously.

At two-year follow-up, pain control remained stable with conservative dosing of BCPlus (in addition to his regular cannabis use), approximately 5 milliliters used as-needed when pain escalates or for prophylactical use such as before 24+ hour absences from home. Two years after initiation of treatment, the patient reports that he now only has fleeting episodes of spasmodic pain, often in the middle three toes, and when the pain begins, he doses with BCPlus sublingually (2-3 ml). Pain relief occurs within two hours. The pain sensations then disappear for 1-6 weeks at a time.

Clinical changes over the past two years:

- Pain Frequency and Severity: Baseline pain occurring "every few seconds of every minute of every hour" has decreased to scattered episodes, with pain-free intervals extending from days to weeks. Current pain episodes rated 6/10 or lower when they occur, contrasting sharply with prior 9/10 episodes.
- Sleep Quality: Complete insomnia during worst pain periods has resolved to normal sleep patterns, with only occasional brief pain-related awakenings.
- Reduction in Anxiety: Early on the patient faced constant physical and emotional tension socially and at work due to uncontrollable painful episodes impacting his ability to relax, deal with stress and interface with others. Now, he feels calm and at ease with significant laughter, feelings of wellbeing, and gratitude.
- Functional Capacity: Social engagement, travel, dating, and leisure activities resumed after years of isolation due to pain.
- Psychosocial Status: Suicidal ideation has completely resolved. Patient reports restoration of life satisfaction and sense of future orientation.
- Orthodox Medication Reduction: Continues single daily tablet of proton pump inhibitor for gastroesophageal reflux disease unrelated to pain condition. He has not used any breakthrough orthodox pain medication or NSAIDs over the past 2 years. His daily use of cannabis and tobacco has continued.

The patient reported excellent consistent relief without developing BCPlus dosage tolerance and no adverse systemic effects. The liposomal formulation demonstrated pleasant taste, flexible dosing and convenient administration route. No drug-drug interactions were identified with the patient's single concurrent medication (proton pump inhibitor).

Patient Feedback

The patient gave the following feedback during the two-year follow-up consultation:

'It has changed my life, in how pain free I am. I have my life back and I'm not screaming in pain anymore. All because of this'.

'I honestly cannot tell you enough what a profound impact it has made to my quality of life in reducing the frequency of that savage, savage pain and the strength of that pain as well…and go about my life without screaming my head off in intractable pain every few seconds- that's embarrassing, that's humiliating, it's demoralizing- and take vacations and take pleasure outings… I've got my life back'

'…it has completely 100% hand on heart made such a huge difference in not just alleviating the horrible symptoms I was getting, the horrible pain I was getting, but enabling me to function and go about my daily life…and that is in so many aspects, whether that's a working life or play or you know having a shower,… catching a train, being in my car or just typing an email…'

Discussion

PLP Pathophysiology

The pathophysiology of PLP is multifactorial, involving complex interactions between the central and peripheral nervous systems (peripheral, spinal, supraspinal mechanisms), as well as psychological factors (stress, anxiety, depression, emotional and cognitive factors) and genetic influences (Wu et al., 2025).

After amputation, nerve fibres at the distal end undergo retrograde degeneration and those at the proximal end sprout to reconnect to the distal end, and during this process, axon regeneration may occur in a disordered way, with resultant neuroma forming at the amputation site (stump). The neuroma can produce spontaneous ectopic discharges, leading to hyperexcitability and allodynia (Wu et al., 2025).

Peripheral sensitization in the dorsal root ganglion (DRG) represents a critical site of pathophysiology, with injured neurons exhibiting altered gene expression, ionic channel dysregulation, and elevated spontaneous activity (Wu et al., 2025). The DRG neurons demonstrate increased neuronal excitability through multiple mechanisms, including altered sodium channel expression (particularly Nav1.8 upregulation), abnormal calcium dynamics, and potassium channel dysfunction (Yeh et al., 2020). The patient's clinical description of pain replication with deep palpation of the stump and persistent phantom sensation in missing digits suggests active dorsal root ganglion sensitization. Prior research indicates that dorsal root ganglia undergo significant molecular remodeling following nerve injury, characterized by downregulation of inhibitory potassium channels and upregulation of excitatory sodium and calcium channels (Yeh et al., 2020).

Wu and colleagues report that the sympathetic nervous system is also involved in development of PLP via sensitization of nociceptors and low-threshold mechanoreceptors, sympathetic coupling in the periphery and DRG as well as other mechanisms (Wu et al., 2025).

Inflammatory responses within the DRG significantly contribute to neuropathic pain development. Peripheral nerve injury induces infiltration of immune cells, microglial activation, and production of pro-inflammatory cytokines including TNF-α, IL-1β, and IL-6 (He & Qiao, 2025). These inflammatory mediators perpetuate neuronal sensitization and maintain chronic pain states. Additionally, upregulation of transient receptor potential channels (particularly TRPV1 and TRPA1) in small-diameter nociceptive neurons enhances pain signal transduction (Gao et al., 2024).

There are several central nervous system (CNS) changes apparent in PLP. This includes cortical reorganization, though research suggests that this is not static and is, rather, dynamic. As Wu and colleagues explain, the thalamus (critical relay centre for sensory and motor information, key role in pain perception) has an important role in PLP, also undergoing reorganization after amputation: neurons originally responsible for the amputated limb's sensory processing now respond to inputs from neighboring body areas, resulting in the misperception of pain in the missing limb (Wu et al., 2025). Central sensitization is also a feature of PLP (Wu et al., 2025).

Finally, PLP is influenced by psychological factors including stress, anxiety and depression which is probably related to neuroinflammation: inflammation, neuroinflammation and oxidative stress have been found to be part of the pathogenesis of anxiety and depression (Guo et al., 2023; Hovatta et al., 2010). Emotional and cognitive factors can contribute to maladaptive cortical reorganization and increased pain perception that occurs in PLP (Wu et al., 2025).

Use of Cannabis for Neuropathic Pain

There are two major phytocannabinoids found in Cannabis sativa, tetrahydrocannabinol (THC) and cannabidiol (CBD) though there are many minor phytocannabinoids (found in smaller amounts). There are many other plant nutrients, including terpenes and terpenoids. These all have their own receptor targets and therapeutic actions. See Baron for further information (Baron, 2018). The term 'entourage effect' is used to refer to the notion that the therapeutic potential of the whole plant is greater than any of its individual components or that the therapeutic effects of the minor phytocannabinoids and terpenes amplifies the effects of THC and CBD (Finlay et al., 2020; Weston-Green et al., 2021).

The patient has been using high THC flower for many years. THC is a partial agonist at cannabinoid 1 receptors (CB1Rs) and cannabinoid 2 receptors (CB2Rs). CB1Rs and CB2Rs are components of the body's endocannabinoid system (ECS). The ECS is a complex cell-signalling, neuro- and immune-modulating system involved in homeostasis of most if not all bodily systems (O'Brien & Blair, 2021). Whilst the cannabinoid receptors are found in many parts of the body including organs and sense organs, skin, nervous system, immune system and so on, CB1Rs are found predominantly in the central nervous system whilst CB2Rs are found in high concentrations in the immune system (cells, tissues, organs) (O'Brien & Blair, 2021). Despite low levels of CB2R expression in the normal central nervous system, evidence shows that the CB2R is involved in many processes at the behavioral level, through both immune and neuronal modulations (Grabon et al., 2023). THC has many therapeutic properties including analgesia, anti-inflammatory, antioxidant and neuroprotective actions and more (O'Brien & Blair, 2021). CBD is also found in cannabis flower; it is also analgesic, and has neuroprotective, anti-inflammatory and antioxidant actions (amongst others), acting predominantly through other receptor targets (it has a low affinity to cannabinoid receptors) (O'Brien & Blair, 2021). Systematic reviews demonstrate efficacy of cannabis and THC in alleviation of chronic pain including neuropathic pain (McDonagh et al., 2022; Mücke et al., 2018; O'Brien & Bosak, 2025; Sainsbury et al., 2021). Tolerance to cannabis and THC can occur, and it is likely that this occurred in this patient who had found that the pain relief he had normally gained from using cannabis had decreased- in his words, it had stopped working.

Based on the research findings from García-Gutiérrez et al. (2018), the CB2R could be a promising target for the treatment of suicide ideation and prevention of suicide due to its distinct expression patterns in the brain's executive centers (García-Gutiérrez et al., 2018). The study identifies significant alterations in both the gene and protein expression of CB2Rs within the dorsolateral prefrontal cortex (DLPFC), a region critical for decision-making and impulse control, of suicide victims (García-Gutiérrez et al., 2018). Crucially, the discovery that CB2R forms heteromers (complexes) with the GPR55 receptor suggests a sophisticated regulatory mechanism where the two receptors mutually influence each other's stability and signaling. These CB2-GPR55 heterodimers may stabilize CB2R function and modulate the neurobiological drivers of impulsivity to stabilize the neural circuits associated with suicidal behavior.

Mechanism of Actions of β-caryophyllene (BCP)

β-caryophyllene (BCP) is a bicyclic sesquiterpene and an active constituent in essential oils derived from a large number of plants such as hops, clove, basil, oregano, rosemary, black pepper, cinnamon, lavender and cannabis (Baron, 2018; Nuutinen, 2018). It is a selective CB2R agonist and has many other receptor targets including PPAR-α and PPAR-γ (agonist), toll-like receptor complexes, 5-HT 1A receptors, ACh receptor (antagonist) and synergises with the µ-opioid receptor pathway (Nuutinen, 2018; Youssef et al., 2019). It has a range of therapeutic actions including antibacterial (e.g., Helicobacter pylori), antioxidant, anti-inflammatory, analgesic (e.g. neuropathic pain, inflammatory pain), anti-neurodegenerative, anticancer, anxiolytic, antidepressant and more (Bahi et al., 2014; Fidyt et al., 2016; Liktor-Busa et al., 2021; Ullah et al., 2021).

Several potential mechanisms of action of BCP appear to be relevant to the PLP. First, BCP is anti-inflammatory and inflammation has been found to be involved in PLP. BCP has been shown to strongly reduce carrageenan-induced inflammatory response in wild mice (but not in mice lacking CB2Rs, indicating that the effect is CB2R-mediated) (Gertsch et al., 2008). BCP-mediated CB2R activation reduces pro-inflammatory cytokine production within DRG tissue. Studies in a diabetic peripheral neuropathy mice model demonstrate BCP dose-dependently reduces TNF-α, IL-1β, and IL-6 levels while simultaneously enhancing IL-10 anti-inflammatory cytokine production (Bagher, 2025). This cytokine rebalancing decreases neuroinflammation-driven neuronal sensitization and may interrupt peripheral-to-central pain signal amplification.

Second, BCP acts through CB2Rs to suppress excitatory ion channel activity in nociceptive DRG neurons. Specifically, CB2R activation modulates voltage-gated sodium channel (Nav1.8) expression and function, reducing neuronal hyperexcitability and spontaneous ectopic activity characteristic of neuropathic pain (Yeh et al., 2020). Additionally, BCP enhances potassium channel activity through CB2R-dependent mechanisms, promoting neuronal hyperpolarization and reduced action potential generation in pain-signaling neurons.

Third, emerging evidence suggests BCP inhibits monoacylglycerol lipase (MAGL) activity (one of the main enzymes to degrade the endocannabinoid 2-arachidonoylglycerol [2-AG]), leading to increased 2-AG levels and consequent CB1R and CB2R activation through both exogenous and endogenous cannabinoid pathways (Klawitter et al., 2024). This dual mechanism—direct CB2R agonism combined with endocannabinoid system potentiation—may contribute to particularly robust analgesia.

Fourth, BCP demonstrates antioxidant properties within DRG neurons, reducing reactive oxygen species (ROS) production and lipid peroxidation that perpetuate neuropathic pain through oxidative damage to neuronal membranes and mitochondrial dysfunction (Ullah et al., 2021). Activation of nuclear factor erythroid 2-related factor 2 (Nrf2) antioxidant response element by BCP upregulates cellular antioxidant defenses including superoxide dismutase and catalase.

Fifth, BCP activates peroxisome proliferator-activated receptors (PPAR-α and PPAR-γ) in addition to CB2Rs, providing complementary anti-inflammatory signaling through these nuclear receptors. PPAR activation further suppresses NF-κB inflammatory pathways and pro-inflammatory gene transcription in both neurons and glia (Baradaran Rahimi & Askari, 2022).

Finally, preclinical research suggests that BCP also has anxiolytic and anti-depressant actions which may also contribute to the experience of pain (Bahi et al., 2014), given that pain is also an affect. Depression is associated with the onset and intensity of PLP, and anxiety can amplify or exacerbate PLP (Wu et al., 2025). CBD has also been found to have anxiolytic and anti-depressant effects (O'Brien & Blair, 2021). However the patient experienced a reduction in anxiety, and suicide ideation completely resolved only after the use of BCP. In rodents, pharmacological activation of CB2Rs under pathological conditions counteracted anxiety- and/or depression- like behaviors induced by chronic stress, neuropathic pain, traumatic brain injury and others (Grabon et al., 2023). As stated previously, BCP is a selective CB2R agonist.

BCP's ability to selectively modulate this excitability profile associated with PLP, reducing sodium channel-mediated depolarization while enhancing potassium channel repolarization, aligns with the clinical observation that symptoms persist but at markedly reduced intensity and frequency. Rather than complete pain elimination, BCP appears to "tone down" the gain of nociceptive signal processing, allowing daily function despite ongoing phantom sensations. This mechanistic understanding may explain why the patient experiences prophylactic benefit when BCP is taken before anticipated stress or extended travel. CB2R-mediated desensitization of DRG neurons reduces the likelihood that triggering factors will generate sufficient depolarization to reach pain threshold, thus preventing symptom escalation.

The efficacy of adjunctive BCP along with cannabis versus prior approaches (gabapentin, opioids) aligns with mechanistic distinctions. Opioids address pain perception through μ-opioid receptor signaling in the central nervous system but do not modify underlying peripheral or spinal sensitization mechanisms. Gabapentin's primary mechanisms involve calcium channel modulation but do not directly address CB2R mediated inflammatory and immune responses central to chronic post-amputation pain. Cannabis contains multiple cannabinoids including major phytocannabinoids (THC and CBD) and many minor phytocannabinoids with varying receptor affinities, however these may lack the CB2R selectivity-optimizing anti-inflammatory effects of BCP (CBD has low affinity for the cannabinoid receptors and THC is a partial agonist at cannabinoid receptors). Whether or not the addition of BCP to the patient's daily high-THC cannabis use was synergistic (ie. 1+1>2) or additive (1+1 =2) is not definitively known, however it is apparent that the adjunct use of BCP was beneficial. BCP may have synergized with CBD contained within the flower: mice research has demonstrated that combining CBD and BCP results in a synergistic analgesic effect involving an inflammatory mechanism (Blanton et al., 2022). Future research in pain models is needed to elucidate if there is an additive or synergistic effect when THC and BCP are combined.

Clinical Implications

This case provides important observations for PLP management:

1. **Pharmacological Heterogeneity:** Individual neuropathic pain conditions demonstrate variable responses to different pharmacological therapies. The patient's poor response to gabapentin and the eventual tolerance to cannabis contrasted sharply with BCP responsiveness when used as an adjunct to his daily cannabis, highlighting the need for novel therapies that target the pathomechanisms underpinning PLP that can provide alternatives to orthodox approaches. BCP is able to address several of the underlying mechanisms of action understood to be involved in PLP.
2. **CB2R-Selective Targeting:** Unlike cannabis or non-selective cannabinoid agonists that can potentially cause psychoactive or addictive effects, BCP's CB2R selectivity provides neuroprotection without these adverse effects. This profile may enhance acceptability and safety particularly in chronic pain conditions requiring long-term management. In the case of this patient who had become tolerant to THC, the addition of BCP may have been additive or synergistic with the major phytocannabinoids in his daily cannabis, resulting in greater pain-relief than use of cannabis alone.
3. **Dorsal Root Ganglion Targeting:** Explicit recognition that post-amputation phantom pain often originates from DRG pathophysiology rather than central mechanisms alone should guide therapeutic approaches. Peripheral targeting of DRG sensitization via CB2R activation represents an underexplored strategy in pain management.

4. **Liposomal Formulation Advantages:** Liposomal delivery enhances bioavailability of BCP through improved membrane permeability and potentially targets drugs to inflamed DRG tissues. Sublingual administration avoids the hepatic first-pass metabolism while providing rapid onset of action.
5. **Behavioral Targeting:** Rapid relief of anxiety, depression and suicidal ideation gave positive incentives to continue the course of BCP therapy with dosage modification. Stress reduction and enhanced sleep calmed neuroinflammation and multiplied the pain relief. Furthermore, the lack of tolerance to BCPlus did not subject the client to any addictive cravings or dependence issues.

Future clinical strategies will be to transition the patient to less harmful routes of delivery of cannabis than smoking (eg. vaporizing flower instead of smoking, oral routes of delivery) and to cut out the use of tobacco with cannabis (which may cause lung cancer). Smoking of cannabis heats the flower to temperatures of around 600-900 degrees Celsius, producing harmful byproducts including tar, polycyclic aromatic hydrocarbons (PAHs), carbon monoxide, and ammonia (MacCallum & Russo, 2018). Chronic inhalation of cannabis has been found to be associated with respiratory symptoms including cough, bronchitis, and increased phlegm (MacCallum & Russo, 2018) but (as yet) there is no definite association between inhaling cannabis and chronic obstructive lung disease (COPD) (Tashkin & Barjaktarevic, 2023) and epidemiological evidence linking cannabis use to lung cancer remains inconclusive, being complicated by factors including concurrent tobacco use, smoking patterns and more (Georgakopoulou et al., 2025). In contrast, vaporizing of cannabis flower heats the flower to much lower temperatures (around 160-230 degrees Celsius) with fewer toxins (CO is reduced, though PAHs are not completely eliminated), and fewer pulmonary symptoms are reported (MacCallum & Russo, 2018). Dietary support of his endocannabinoid system can include addition of healthy fats (eg. olive oil, and/or sources of omega-3 polyunsaturated fatty acids) and Palmitoylethanolamide (PEA) powder. PEA is a naturally occurring fatty acid amide, part of the body's extended endocannabinoid system, that has shown promise in the treatment of peripheral neuropathic pain (D'Amico et al., 2020). In human studies PEA has been shown to be effective in treatment of chronic pain, including neuropathic and inflammatory pain, as well as improving sleep, quality of life and well-being (Lang-Illievich et al., 2023; Scuteri et al., 2022). Oral delivery of cannabinoids may also be considered and may be useful for his chronic condition- whilst the onset of action is longer for the oral route of delivery (60-180 minutes) than the inhalation route (5-10 minutes), duration of action for the oral route is longer (6-8 hours) than the inhalation route (2-4 hours) (MacCallum & Russo, 2018).

Research Recommendations

There is little clinical research into the efficacy of BCP either alone or in conjunction with other therapies such as MC. Much of the research is preclinical. Future research should include randomized controlled trials of BCP with and without MC, including in comparison with standard pharmacotherapy (eg. gabapentin, duloxetine, pregabalin) in post-amputation pain populations to provide rigorous efficacy and safety data. Longer-term prospective observational studies are needed to establish long-term safety profile and assess for tolerance development or adverse effects emerging over months-to-years of continuous use of BCP. Preclinical research that assesses the potential effects of BCP on human DRG neuronal excitability, inflammatory markers in cerebrospinal fluid, and functional neuroimaging of pain-related brain regions would further elucidate mechanisms of action of BCP. Dose-titration studies would be useful to optimize dosing schedules (prophylactic versus as-needed) and individual patient factors predicting response wo auld refine clinical application.

Conclusion

This case documents substantial and sustained improvement in treatment-refractory post-amputation phantom limb pain using a liposomal BCP formulation as an adjunct to MC, suggesting a potentially beneficial synergistic or additive effect with THC and CBD. The patient's dramatic functional restoration and elimination of suicidal ideation suggests that BCP's clinical impact extends beyond pain management. It is possible that in relation to the suicide ideation, which may be behavioural and/or inflammatory in nature, BCP may be acting directly on CB2Rs in the brain as well as via anti-inflammatory effects, though at this point, this is speculation and more research is warranted.

BCP's multi-targeted mechanisms- CB2R activation, inflammatory cytokine suppression, ion channel modulation, oxidative stress reduction, and PPAR activation- align coherently with known neuropathic pain pathophysiology, particularly dorsal root ganglion sensitization. While this represents a single case requiring confirmation through larger trials, the observation warrants attention from pain specialists and suggests that selective CB2R agonists may represent a novel therapeutic avenue for post-amputation pain syndromes resistant to conventional pharmacotherapy. This case study suggests that BCP has potential as a novel therapeutic approach for refractory post-amputation pain syndromes, in conjunction with MC. Further research into BCP with and without cannabis in PLP in the future is warranted.

Declarations and Disclosures

Philip Blair, MD, is the CEO of Blair Medical Group, SPC, which provided the BCP product used in this case study. The remaining author declares no competing interests.

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