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Issue Summary

Biointelligent Dentistry: A Paradigm Shift

Cooper DL, Cassidy JP, Editors*

PhytoDental Solutions Inc., Homosassa, FL, USA

Issue Overview

Cooper DL* and Magyar CW

PhytoDental Solutions Inc., Homosassa, FL, USA

*Corresponding author: David L Cooper, PhytoDental Solutions, Inc., Homosassa, Florida 34446, USA, E-mail: david@phytodentalsolutions.com

Summary

We have completed a series of clinical studies all utilizing two advanced patented nanochemistry delivery systems [1-5]. Both the original CBD isolate based nanoemulsion formulation (Cannabidiol Anti-Inflammatory Rinse, CAIR) [6] and later our refined micellar broad spectrum phytocannabinoid based preparation (Phytocannabinoid Ant-Inflammatory Rinse, PAIR) [7-9] as the actives, indicate the importance of evaluating the Oral Systemic Health Ecosystem [10]. Additionally, we and our collaborators have shown that the broad-spectrum micellar phytocannabinoid formulations has multiple positive systemic effects managing inflammation, cardiovascular health markers, diabetes, neuropsychiatric [11,12] and may play a role in decreasing the incidence of diseases associated with hyperinflammation [13]. Maintaining the Oral Systemic Well Health Ecosystem is a singular effort not one to be broken in two to be managed independently by physicians and dentists. Understanding how to utilize the biologically conserved roles [14] the phytocannabinoids play in both the oral and systemic milieu will lead to increasingly advantageous well dental health and systemic health strategies.

Section 1: BioIntelligent Dentistry

1. *Modeling the Biological Mechanisms of Phytocannabinoids in Dental Health and Disease* (Cooper and Magyar)

The focus of this paper is to elucidate the multiple molecular underpinnings exploited in development of new treatment approaches for the dental operatory. Beginning with an understanding of the hemp plant's phytocannabinoids direct-acting biological activities has resulted in development of products proven effective across multiple dental diseases and procedures. Focus on the plant's evolutionarily conserved biological activities to maintain the capabilities of man's oral microbiome improves oral health naturally. This is in contrast to dentistry's historic reliance on commercial pharmaceuticals or the application of industrial chemicals classified as antiseptics and quaternary ammonium compounds (QACs) to treat oral disease. The science-based approach presented in this paper should be a truly welcome and notable disruptive advancement to the practice of dentistry by dental professionals and their patients alike. Modeling the Biological Mechanisms of Phytocannabinoids in Dental Health and Disease is the first step in the paradigm shift towards the practice of BioIntelligent Dentistry.

Section 2: Manufacturing Nano Chemistries

2. Development of a CBD Nanoformulation.

3. Technical Advance: Development of a Micellular full Spectrum Hemp Formulation and *Ex Vivo* Characterization.

4. Human Cannabinoid Pharmacokinetics.

Development of a CBD Nanoformulation. **(Chauhan, Christopher and Lanier).**

Cannabidiol (CBD) is considered to have many medicinal properties which are leading to efforts to develop effective methods of delivery. CBD is a hydrophobic molecule, i.e., it has very limited solubility in water. Therefore, dispersing it in aqueous formulations is not an effective approach for treating diseases. Nanoparticles of CBD or CBD mixed with other inactive components can be dispersed in aqueous formulations to formulate what is typically referred to as "water soluble" CBD, though a more accurate term would be "water dispersible" CBD. These types of formulations retain stability for long times and increase bioavailability of dosed orally compared to control (non-nano) CBD formulations. This publication discloses a novel composition and a method of "water soluble" CBD.

Technical Advance: Development of a Micellar Full Spectrum Hemp Formulation and ex vivo Characterization. **(Smith, Cooper, and Sorensen)**

Phytocannabinoids, such as cannabidiol (CBD) and tetrahydrocannabinol (THC), are highly lipophilic compounds with poor aqueous solubility and bioavailability. Several formulation techniques have been explored to enhance the solubility and bioavailability of phytocannabinoids, including liposomal encapsulation, nano-sizing, and micellization. Among these, micellization presents distinct advantages, supported by emerging clinical validation. Cannabis sativa is the predominant strain used in cannabinoid-based products today, and clinical studies on micellar formulations primarily focus on this strain. However, the principles of micellar solubilization are applicable across other cannabis species/strains. This study investigates a proprietary micellization process, Purzorb® technology, which solubilizes full-spectrum hemp oil for oral

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***Correspondence:** Cooper DL, PhytoDental Solutions Inc., Homosassa, FL, USA

and topical administration. An animal model using a Franz diffusion apparatus demonstrated 85% absorption through the intestinal lining, significantly outperforming traditional CBD oil. Two human pharmacokinetic studies assessed bioavailability, with one showing rapid appearance in the blood within 15 minutes and sustained near maximal blood concentrations over 8 hours, and another a 60-day trial confirming reductions in inflammation and improvements in sleep, anxiety, and pain. These findings suggest micellar formulations offer superior bioavailability, faster onset, and prolonged effects, with potential applications in metabolic disorders, neuroinflammation, pain management, sleep disorders, and oral health.

Human Cannabinoid Pharmacokinetics: Purzorb® Full Spectrum CBD Oil (Hempzorb®). **(Smith, Sorensen, Cooper and Cassidy)**

The onset of Purzorb® is rapid and it has a lasting duration of CBD availability in the blood stream following sublingual/swallowing administration. All the patients demonstrated CBD in their blood stream by the first measurement of 15 minutes which was approximately 50% of the maximum concentration (Cmax). The Cmax was maintained from 45 minutes through approximately 8 hours post administration. The rapid appearance within the blood stream approaches what has been shown with CBD or THC that has been inhaled or vaped; however, Purzorb produced sustained concentration that lasts for approximately 8 hours. The blood levels measured were significantly higher than what has been seen with standard CBD oil and other solubilizing methods. From these studies, it is concluded that the uptake of Purzorb® CBD far exceeds the average uptake of CBD products available on the market today.

Section 3: Foundational Clinical Papers (Early Work)

5. Anti-Inflammatory Activity of Cannabidiol Anti-Inflammatory Rinse (CAIR) and Gels (CAIG) in the Treatment of Oral Pathologies Including Chronic Systemic Underlying Disease States.

6. Pilot Clinical Trial Validates the Safety and Efficacy of Micellar Deliver of a Full Spectrum Phytocannabinoid Formulation.

Anti-Inflammatory Activity of Cannabidiol Anti-Inflammatory Rinse (CAIR) and Gels (CAIG) in the Treatment of Oral Pathologies including Chronic Systemic Underlying Disease States **(Magyar and Cooper).**

A series of case studies, spanning common gingivitis to severe periodontal disease, were treated with a Cannabidiol Anti-Inflammatory Rinses (CAIR) and Cannabidiol Anti-inflammatory Gel and put parenthesis around CAIG. Patients were followed using bleeding on probing (BOP) and periodontal pocket depth (PPD) to empirically measure effectiveness of CAIR treatments. The goal of this study was to expand the clinically recognized activity of phytocannabinoids. The results presented here show the CAIR and CAIG to be effective anti-inflammatory treatments option across a spectrum of dental diseases, including those with the multiplier effect of an underlying inflammatory disease that was systemic in origin. In cases of serious underlying systemic disease our results indicate CAIR treatment is a useful palliative treatment capable of substantially improving a patient's quality of life.

Pilot Clinical Trial Validates the Safety and Efficacy of Micellar Deliver of a Full Spectrum Phytocannabinoid Formulation. **(Chong, DeSilva, Levin, Steinburg, Burbidge, Smith and Cooper).**

This study evaluates a panel of biomarkers which are associated with two significant areas of interest explored by others for application of phytocannabinoid formulations. These are biomarkers associated with systemic inflammatory processes and a second panel of biomarkers related to cholesterol, lipid and sugar metabolism as prognostic risk factors for diabetes, a disease process with a large inflammatory component. In this study, utilizing this overlapping biomarker panel we evaluated the systemic safety of CBD delivered as a component of a CBD broad spectrum micellar phytocannabinoid formulation Hempzorb81®. We report here the effects at Day 60 including: (a) decreased anxiety and joint pain; (b) statistically significant reductions in the inflammatory markers including tissue necrosis factor α (TNFα) and interleukin (IL)-6 (p-value 0.03) and reduced erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) levels; (c) hemoglobin (Hb)A1c markedly decreased on average 1.0 mmol at 90 days; and (d) homocysteine reduced by 20% (p-value 0.02). These finding indicate a potential role for Full Spectrum Hemp Oil micellized by Purzorb® technology as a potential adjuvant or natural plant product alternative treatment for both inflammatory and diabetes related diseases. There were no reported untoward effects of any type reported by subjects for the length of the study. Therefore, we conclude that Full Spectrum Hemp Oil (Med7) was shown by our empirics and clinical oversight to be a safe and effective formulation in this Pilot study.

Section 4: Clinical Investigations

7. Dose Escalation Study: DenticDS™ PAIR Versus Placebo in Adult Patients with Gingivitis

8. Theory Of Baseline Health. Utility Of Magyar Curves

9. Dental Anxiety Management by Full Spectrum CBD Formulations: Dual Dosing (AM/PM) Protocol in a Real-World Setting

10. Approaching Dental Anxiety: Importance, Measurement and Recent Advance in Management of the Oral Health to Systemic Disease Ecosystem

11. Anti-Inflammatory Activity of a Full Spectrum CBD-Rich Hemp Formulation in Patients with Covid-19 Infection

Dose Escalation Study DenticDS™ PAIR versus Placebo in Adult Patients with Gingivitis. **(Magyar and Cooper).**

The buccal oral mucosal barrier (BOMB) is a major anatomic line of defense against oral pathogens gaining entry into the systemic blood and lymphatic systems. In patients suffering from moderate to severe gingivitis a three-dose escalation study with twice daily treatment by a phytocannabinoid anti-inflammatory rinse (PAIR) reduced empiric measured bleeding points by over 75% at the highest dose within 2 weeks. Such a reduction in gingival inflammation and bleeding significantly hardens/improves the oral mucosal barrier to prevent pathogen entry into the systemic blood and lymphatic systems.

Theory of Baseline Health- Utility of Magyar Curves. (Cooper and Magyar).

In patients with remarkable systemic inflammatory processes,

considering the systemic process as a potential major determinant of their current and future dental disease state is a critical determinant to address when managing the patient's clinical course. Therefore, utilizing the concept of a patient's baseline health will improve the clinicians understanding of each patient's responsiveness to and guide treatment. Magyar curves generated over extended periods of time on multiple empiric determinants is one visualization analysis which may prove of utility. Application of appropriate Artificial Intelligence apps to retrieve, analyze and structure archival information may quickly bring analysis such as this to the operatory.

Cooper DL, Stephan R, Maygar CW. *Dental Anxiety Management by Full Spectrum CBD Formulations: Dual Dosing (AM/ PM) Protocol in A Real-World Setting.* Clin Med. 2021;3(2):1038.

Cooper DL, Maygar CW. *Approaching Dental Anxiety: Importance, Measurement and Recent Advance in Management of the Oral Health to Systemic Disease Ecosystem.* Clin Med. 2022;4(1):1041.

Up to 20% of dental patients suffer varying degrees of anxiety when faced with dental visits and procedures. Chronic non-compliance with prescribed dental care and maintenance is associated ultimately with poor dental health. Current pharmacologic treatments such as benzodiazepines for Dental Anxiety are associated with poor efficacy and significant side effects. To measure the level of patient's Dental Anxiety the self-reporting PhytoDental Solution's Dental Anxiety Scale (PDSDAS) was developed.

Subjects were provided with two decarboxylated full spectrum hemp CBD oral formulations (i.e. Purzorb^{R}). The PM dose formulated to assist with relaxation and sleep the night before. The AM dose formulated to calm the patient the day of the procedure to be taken approximately 15 minutes before arrival at the dentist's office.

Application of a Dual Dosing AM/PM Protocol, now DenticDS^{TM} Patient Comfort Daytime and Nighttime, found the phytocannabinoid based formulations to be effective Dental Anxiety anxiolytics. Anxiety is the #1 worldwide mental illness with Dental Anxiety the fifth leading cause. Dental fear may produce a vicious cycle where dental problems are not adequately serviced as the patient no longer can face the symptom-driven treatment when faced with the threatening stimuli perceived with in-office dental care and procedures. The Dual Dosing (AM/PM) Protocol is PhytoDental Solutions' approach to Dental Anxiety Management.

Montgomery M, Smith GL, Burbidge SK, DeSilva Jr D, Cooper DL. *Anti-Inflammatory Activity of a Full Spectrum CBD-Rich Hemp Formulation in Patients with COVID-19 Infection.* Clin Med. 2022;4(1):1042.

The coronavirus disease-19 (COVID-19) pandemic is attributable to the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). The pathogenesis of SARS-CoV-2 is attributed to the activation of multiple inflammatory pathways secondary to the interaction of virus and host immune responses. In patients over the age of 60, most with one or more underlying conditions, are at increased risk of undergoing the pathophysiologic process of hyper-inflammation and its accompanying Cytokine Storm Syndrome (CSS) which results in significant morbidity and mortality. Therapeutics which reduce the release of inflammatory cytokines have been sought to slow disease progression.

A growing body of literature attests to the anti- inflammatory effects of the naturally occurring cannabinoids found in both cannabis and hemp plants. The major cannabinoid, cannabidiol (CBD) results in decreased cytokine production via Cannabinoid receptor 2 (CB2) and protect against infection by inducing anti-viral activity. This study of Hempzorb81^{TM}, a highly bioavailable micellar cannabinoid-rich CBD full spectrum phytocannabinoid formulation compared the anti-inflammatory effects of treatment of 44 study subjects who tested positive for COVID-19 infection compared to a 39 subject COVID-19 negative test control group. TNFα, CRP, IL-1,6 and White Blood Cell count (WBC) all showed positive improvement with statistically significant p-values in the COVID-19 positive cohort. In the course of the study, no COVID-19 positive patients were hospitalized or died. A 2-fold reduction in white blood cell count at the time of diagnosis over the treatment course was an additional significant indicator for improved outcome post-infection.

As one of the first human subject studies evaluating CBD hemp-based formulations in COVID-19 test positive patients, substantial evidence was developed to consider highly bioavailable CBD cannabinoid-rich formulations as useful potential adjuvants to recognized palliative and therapeutic options for COVID-19 infections and potentially other hyperinflammatory states.

Section 5: Latest Lessons: Real World Utility in the Dental Operatory

12. Phytocannabinoid Dental Products Exhibit Widespread Clinical Utility in the Generalist's Dental Operatory.

13. Novel Approach to Anxiety Management: Collaborative Opportunity Medical and Dental Professionals.

***Phytocannabinoid Dental Products Exhibit Widespread Clinical Utility in the Generalist's Dental Operatory.* (Sanchez Garrido).**

A series of case studies illustrate that Phytocannabinoids possess multiple properties applicable to dental disease. These include anti-inflammatory reduction in pro-inflammatory molecules such as TNF-α and IL-1.6, anti-microbial activity including against MDR staph aureus, and collagen stimulation important in wound healing. To date we have successfully utilized phytocannabinoid anti-inflammatory rinse (PAIR) Rinse with mild and moderate gingivitis even in the face of significant systemic inflammatory processes, lichen plans, thrush, mucosal sores from physical irritation, post-chemotherapeutic oral mucositis and the painful effect of post- whitening procedures. PAIR is also our rinse and irrigant of choice, reducing irritation and discomfort associated with scaling and root planning. PAIR supports the oral microbiome's commensal bacteria necessary to maintain oral health. PAIR further supports fibroblasts and collagen production unlike chlorhexidine and alcohol-based mouth rinses. This product has wide utility in the dental operatory!

***Anxiety Management: Collaborative Opportunity Medical and Dental Professionals.* (Magyar and Magyar)**

Multiple patients suffering from anxiety present routinely to the dental operatory. The etiology of all patients in this study were unrelated to dental anxiety and were of mixed origin. In this report we summarize the surprising response of 3 individuals provided with three formulations developed for continuous care of dental implant patients which contain anxiolytic ingredients. Medical analysis of

these patients indicates essential underlying processes associated with global causes of anxiety gives impetus to dentists to utilize new treatments, such as described here, as they become available. Situational awareness, recognition and successful treatment of the anxious patient reinforces the critical shared role dentists and physicians play in providing health care.

Conclusion

The accelerating understanding and emphasis on the interaction between oral and systemic disease on each other has resulted in uncovering associations across a wide spectrum of diseases. From the correlation of oral microbiota to pneumonia and atherosclerotic disease to accumulating evidence linking oral bacteria to mental and neurological disease including Alzheimer's and Multiple Sclerosis, maintenance of the buccal oral mucosal barrier (BOMB) is seen as critical in maintaining Dental Well Health within the Total Well Health continuum. There may be no more important reason to maintain the integrity of this interface than what the WHO declares dental disease is the #1 infectious worldwide and is a major contributor to the #1 Worldwide health threat to man by the continued emergence of drug-resistant organisms following dental treatments with broad spectrum antibiotics of decreasing utility.

Key to maintaining the BOMB barrier is understanding the complementary role played by the endocannabinoid system (ECS) on oral tissues and systemic circulatory and organ systems. Improving our understanding the distinct roles played by the cannabinoid family of molecules in health and disease is another key. Although cannabinoids such as CBD interact with receptors in both the mouth and systemically, major differences are becoming increasingly apparent. In the mouth, specific pharmacologic effects including anti-inflammatory, anti-microbial with collagen formation stimulating tissue repair and healing are initially a mucosal surface interaction reducing the effect of TNFα, IL-1,6 and controlling pathogenic microbiome components of the oral microbiota from systemic entry.

Systemically, various cannabinoids including CBD have been shown to also exhibit anti-inflammatory effects in diseases such as diabetes. However, when delivered systemically cannabinoids interact with a broad range of known (CB1, CB2, etc.) and unknown or poorly characterized receptors. The combined effects of interactions across these receptors specifically when broad or full spectrum preparations are utilized has been simplistically accepted as the "entourage" effect. However, we agree the effect of such preparations is more accurately explained by traditional pharmacological terms pertaining to other plant-based medicinal products and polypharmacy in general (e.g., synergistic interactions and bioenhancement).

Together, this Special Issue of Clinics in Medicine highlights a proposed role for the natural plant phytocannabinoids in maintaining the integrity of the buccal oral mucosal barrier as well as influencing multiple well-health systemic and inflammatory markers as the keys to establishing/managing a patient's overall health. There were no reported side effects or drug interactions reported in any study to these broad-spectrum Phytocannabinoid formulations. The developing new paradigm in dental practice is the goal of providing Continuous Care™ based on the concepts of Precision Dentistry and Personalized Care. Utilization of a safe, effective micellar broad-spectrum phytocannabinoid formulations, augmented appropriately to the patient's need, appears capable of playing a central or adjuvant role in the development of Oral-Systemic Health Care programs.

Looking Forward

To bring phytocannabinoid products into conventional medicinal products, solid clinical evidence-based data sets need to be developed to support dentists and physicians in their preparation of an effective treatment plan for their patients. In the papers of this dedicated issue, we are demonstrating the commitment to empirically developed measurements of phytocannabinoid product safety and efficacy. Today's conventional, legacy regulatory approval standards for bringing pharmaceutical products to consumers, however, continues to leave many with unmet medical needs for even the largest clinical oral-systemic indications such as diabetes and periodontal disease.

Regulatory requirements historically have dictated a drug candidate consisting of multiple active pharmaceutical ingredients need demonstrate superior efficacy or safety over the individual components. This requirement is an extraordinarily high bar for natural biological plant extracts. Investigators in the field of cannabis therapeutics have described the potential of phytocannabinoid and terpene combinations for specific clinical indications. Advancement of understanding the particularly important combination of active molecules may represent in the future a new definition of the regulatory gold standard term "predicate" for plant-based product development. The unique combinatorial effect of exact combinations of phytocannabinoid formulations, i.e. cannabinoids, terpenes and flavonoids, will be validated by pre-clinical and clinical studies for pharmacologic safety and efficacy.

Alternatively, the FDA has approved two products (Veregen® (sinecatechins topical ointment, Fougera Pharmaceuticals, Inc.) and Mytesi™ (crofelemer oral delayed release tablets, Napo Pharmaceuticals, Inc.) under a Botanical Drug Guidance [15]. In essence, application is made through the 505(b)(2) pathway. This allows botanical products to be regulated as drugs with the full intended use labeling including diagnosing, curing, mitigating or preventing disease. The Guidance recognizes botanical drug products are complex molecular mixtures with purification and identification of active ingredients as optional. The FDA notes interpretation of standard chemical regulatory definitions need extending to accommodate the complex nature of plant extracts. Consistent with 505(b)(2) applications, previously published data such as clinical studies indicating consistent therapeutic efficacy and safety in place of nonclinical toxicity studies may be used. The FDA has also acknowledged it is revising its policy of combination drug products to facilitate the development of new botanical drugs stating- "natural mixtures in a single part of a single plant will not be considered as a fixed combination drug product and thus is not subject to the combination requirement." Such an evolving approach to regulatory approval of botanical drugs by the FDA may be seen as the critical step in the eventuality of regulatory allowances for a more-timely development of plant-based multi-active components for clinical utilization. However, additional information including source of raw materials and other non-CMC data including species identification, geographic location, processing and available bioassays will still be required.

References

1. Smith M, Cooper Dl, Sorensen C. Technical advance: Development of a micellar full spectrum hemp formulation and *in vivo* characterization. Clin Med. 2025;7(1):38-41.

2. Smith M, Sorensen C, Cooper DL and Cassidy J. Human cannabinoid pharmacokinetics product: Purzorb® Full Spectrum CBD Oil (Hempzorb®). Clin Med. 2025;7(1):45-7.

3. Chauhan A, et al. Development of a CBD Nanoformulation. Clin Med. 2025;7(1):14-20.
4. Sorensen C, Montgomery M, Smith M. Micelle preparations of full-spectrum hemp oil. US Patent: 20230038771 A1. 2024.
5. Chauhan A. Nanosuspensions of Cannabidiol for Developing Water-dispersible Formulations. US Patent:11975098 B2. 2024.
6. Magyar CW, Cooper DL. Anti-inflammatory activity of Cannabidiol Anti-Inflammatory Rinse (CAIR) and Gels (CAIG) in the treatment of oral pathologies including chronic systemic underlying disease states. Clin Med. 2025;7(1):8-14.
7. Cooper DL, Magyar CW. Dose escalation study DenticDSTM PAIR vs. placebo in adult patients with gingivitis. Clin Med. 2025;7(1):21-3.
8. Magyar CW, Preston V, Goff Y, Smith C, Cooper DL. Innovations in dental health: DenticDS™ PAIR Rinse utilizes dual nanochemistries. Inside Dentistry. 2024;eNL.
9. Sanchez Garrido N. Phytocannabinoid dental products exhibit widespread clinical utility in the generalist's dental operatory. Clin Med. 2025;7(1):34-7.
10. Cooper DL, Maygar CW. Approaching dental anxiety: importance, measurement and recent advance in management of the oral health to systemic disease Ecosystem. Clin Med. 2022;4(1):1041.
11. Chong C, DeSilva. Pilot clinical trial validates the safety and efficacy of a full spectrum phytocannabinoid micellar formulation. Clin Med. 2025;7(1):51-6.
12. Cooper DL, Stephan R, Maygar CW. Dental anxiety management by full spectrum CBD formulations: dual dosing (AM/ PM) protocol in a real-world setting anesthesia and patient safety. Clin Med. 2021;3(2):1038.
13. Montgomery M, Smith GL, Burbidge SK, DeSilva Jr D, Cooper DL. Anti-inflammatory activity of a full spectrum CBD-rich hemp formulation in patients with COVID-19 infection. Clin Med. 2022;4(1):1042.
14. Cooper DL, Magyar CW. Review: Modeling the biological mechanisms of phytocannabinoids in dental health and disease. Clin Med. 2025;7(1):24-33.
15. Botanical Drug Development Guidance for Industry. 2016. FDA.gov.

Physician's Commentary

Natural Plant Phytocannabinoids offer New Tools for Physicians and Dentists to Fight Disease

Janice Knox

Founder and CEO, Doctors Knox, Inc.; Founder, Abena IHR; President, DK Technologies, Inc.

Dental disease affects approximately 3.5 billion people worldwide, constituting the most prevalent infectious disease globally [1]. Despite technological advances in dentistry, traditional approaches to managing oral infections and inflammation rely heavily on antiseptics and antibiotics that disrupt the natural oral microbiome and potentially contribute to antimicrobial resistance [2,3].

In the ground breaking review in this issue, "BioIntelligent Dentistry - Modeling the Biological Mechanisms of Phytocannabinoids in Dental Health and Disease," Cooper and Magyar [4] explore how phytocannabinoids derived from hemp offer a promising alternative through their multi-faceted biological mechanisms. Unlike conventional antiseptics that indiscriminately kill oral bacteria, phytocannabinoids selectively target pathogens while preserving beneficial microbiota. They also exhibit potent anti-inflammatory properties by modulating cytokine production [5,6] and promote tissue healing by stimulating fibroblast activity and collagen formation [7].

The authors highlight the evolutionary connection between plant and human defense systems, explaining why phytocannabinoids effectively interact with the human endocannabinoid system to strengthen oral mucosal barriers. This interaction not only addresses local oral health issues but also prevents the transmission of oral pathogens to systemic circulation, potentially reducing the risk of related cardiovascular, respiratory, and other systemic diseases [8,9].

Their innovative DenticDS™ PAIR rinse represents a shift from chemical antiseptics toward biologically-aligned phytocannabinoid formulations that work with the body's natural mechanisms rather than against them. This approach promises to transform dental care by addressing the limitations of current treatments and offering a more balanced solution to oral health maintenance.

Information provided in this Special Issue of Clinics in Medicine is a clarion call to physicians and dentists alike. With our improved understanding of the interrelationship particularly of the oral and gut microbiomes, provision of continuous health care [10] is a collaborative effort incumbent upon both professions to participate.

As a member of a family of practicing Cannabinoid physicians we understand and fully support this vision.

References

1. World Health Organization. Oral Health. 2025.
2. Heta S, Robo I. The Side Effects of the Most Commonly Used Group of Antibiotics in Periodontal Treatments. Med Sci. 2018;6(1):6.
3. Arnold WA, Blum A, Branyan J, Bruton TA, Carignan CC, Cortopassi G, et al. Quaternary Ammonium Compounds: A Chemical Class of Emerging Concern. Environ Sci Technol. 2023;57(20):7645-65.
4. Cooper D, Magyar W. Novel Approach to Anxiety Management or BioIntelligent Dentistry? Collaborative Opportunity Medical and Dental Professionals. Clin Med. 2025;7(1):14-20.
5. Garzon HS, Loaiza-Oliva M, Martínez-Pabón MC, Puerta-Suárez J, Corral MAT, Bueno-Silva B, et al. Antibiofilm and Immune-Modulatory Activity of Cannabidiol and Cannabigerol in Oral Environments-In Vitro Study. Antibiotics. 2024,13(4):342.
6. Jirasek P, Jusku A, Frankova J, Urbankova M, Diabelko D, Ruzicka F, et al. Phytocannabinoids and gingival inflammation: Preclinical findings and a placebocontrolled double-blind randomized clinical trial with cannabidiol. J Periodont Res. 2024;59(3):468-79.
7. Scutt A, Williamson EM, Cannabinoids stimulate fibroblastic colony formation by bone marrow cells indirectly via CB2 receptors. Calcif Tissue Int. 2007;80(1):50-9.
8. Bale BF, Doneen AL, Vigerust DJ. High-risk periodontal pathogens contribute to the pathogenesis of atherosclerosis. Postgrad Med J. 2017;93(1098):215-20.
9. Park DY, Park JY, Lee D, Hwang I, Hye-Sung Kim. Leaky Gum: The Revisited Origin of Systemic Diseases. Cells. 2022;11(27):1079.
10. Magyar CW, Preston V, Goff, Y, Smith C, Cooper DL. Innovations in Dental Health: DenticDS™ PAIR Rinse Utilizes Dual Nanochemistries. 2024.

Dentist's Commentary

Cannabinoids for Collaborative Care

Dr. Hindin

President, American Academy of Physiological Medicine and Dentistry; Director, Foundation for Airway Health

There is growing awareness that what happens in the mouth does not always come from the mouth and what happens in the mouth can affect what happens in the rest of the body. The medical-dental connection is an important part of this movement especially in the recognition of increasing numbers of adults with multiple chronic conditions [1] and our continued lag behind other countries to improve the overall health of our people.

Oral conditions such as caries, periodontal disease, temporomandibular joint (TMJ) dysfunction, chronic infections, and airway/sleep disorders have been found to be not only risk factors, but in some cases direct causes of the chronic diseases plaguing all ages. For example, *Porphyromonas gingivalis,* a bacterial pathogen in periodontal disease, has been found in the plaque of cardiovascular disease and Alzheimer's [2,3].

In the healthcare siloed world, dentistry treats periodontal disease with improved home care, periodic deep cleaning, oral rinses and surgery. A newer approach incorporates these same modalities and considers oral pH, the microbiome [4], Autonomic Nervous System (ANS) balance, sleep and airway, stress management and cortisol, nutrition, and more. Lab tests such as CRP, HbA1c, ESR, IL-6 are ordered, and dentists refer and confer with their medical colleagues.

Instead of waging a war of scraping, cutting and burning the bacteria; good and bad from the oral environment, there is a growing shift in focus to making the oral terrain less hospitable for pathogens and restoring a healthy microbiome, proper pH, and utilizing a collaborative team approach with physician colleagues to discover and treat all existing factors.

In this issue, a new treatment utilizing products from the world of phytocannabinoids shows promise in providing a treatment approach that restore balance by modulation of various physiological processes and bridges the medical dental world. Multi-authored manuscripts of originally published material emphasizes the years of effort invested into technology, biological sciences, advanced chemistries and clinical studies necessary to bring this next potential breakthrough [5] to the

dental operatory.

The world of phytocannabinoids offers great promise for restoring oral balance and for those patients and practitioners working collaboratively to prevent and reverse the epidemic of chronic disease. We agree with the authors expanded vision, to emphasize the need of dentists and physicians and all associated health care professions will be necessary if we are to establish and manage the continuing care of dental patients spanning hygiene and procedural intervention.

References

1. Boersma P, Black L, Ward BW. Prevalence of Multiple Chronic Conditions Among US Adults, 2018. Prev Chronic Dis. 2020;17:E106.
2. Mougeot J-LC, Stevens CB, Paster BJ, Brennan MT, Lockhart PB, Mougeot FKB. Porphyromonas gingivalis is the most abundant species detected in coronary and femoral arteries.
3. J Oral Microbiol. 2017;9(1):1281562.
4. Lei S, Li J, Yu J, Li F, Pan Y, Chen X, et al. Porphyromonas gingivalis bacteremia increases the permeability of the blood-brain barrier via the Mfsd2a/Caveolin-1 mediated transcytosis
5. pathway. Int J Oral Sci. 2023;15(1):3.
6. Yu X, Devine DA, Vernon JJ. Manipulating the diseased oral microbiome: the power of probiotics and prebiotics. J Oral Microbiol. 2024;16(1):2307416.
7. Commentary. Knox J. Clin Med. 2025;7(1):14-20.