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Letter to the Editors

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When ‘Cannabidiol’ Is Not Cannabidiol — And Why It Matters for Clinicians and Patients

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Introduction

Cannabidiol (CBD) has emerged as one of the most widely prescribed and consumed cannabinoid-based interventions worldwide, and Brazil has been no exception to this global expansion. Originally approved for rare paediatric epileptic syndromes and subsequently investigated across an expanding spectrum of psychiatric and medical conditions, CBD has acquired a reputation as a safe, non-intoxicating, and comparatively well-tolerated therapeutic agent [1,10]. However, the rapid expansion of CBD use has created a clinically important paradox: evidence generated with rigorously characterised cannabidiol is increasingly extrapolated to products that may differ substantially from those actually studied. A fundamental problem therefore remains underappreciated in both clinical and regulatory discourse—in Brazil and internationally: many products marketed as “CBD” bear little pharmacological resemblance to the rigorously characterised cannabidiol evaluated in controlled

clinical trials [2]. This is not simply a matter of nomenclature or pharmaceutical quality. It directly affects the interpretation of efficacy, attribution of adverse events, dosing, drug interactions and, ultimately, the benefit–risk assessment made by clinicians and patients.

The Heterogeneity of “CBD” Products

The term “CBD” is increasingly employed as an umbrella term encompassing highly heterogeneous preparations that differ substantially in cannabinoid composition, purity, manufacturing standards, route of administration, bioavailability and contaminant profiles [2]. Pharmaceutical-grade CBD formulations—such as Epidiolex®—are produced under rigorous Good Manufacturing Practice (GMP) standards and contain a precisely characterised single-molecule active ingredient. By contrast, many commercially available products consist of botanical extracts containing variable and frequently uncharacterised concentrations of cannabinoids, terpenes and flavonoids, and may additionally contain residual solvents, pesticides, heavy metals, microbial contaminants and other unidentified constituents [3]. Consequently, two products marketed as “CBD” may represent fundamentally different pharmacological interventions—a distinction seldom emphasised in clinical discussions and frequently overlooked in research and medical practice. The clinical consequence is straightforward but potentially serious: prescribing a nominal dose of “CBD” does not necessarily mean prescribing a known dose of cannabidiol, nor does it ensure exposure to cannabidiol alone.

Labeling Inaccuracy: An Enduring Problem

Multiple independent investigations have documented substantial and clinically relevant discrepancies between labelled and actual cannabinoid content in commercially available CBD products. In the landmark study by Bonn-Miller et al. [4], nearly 70% of CBD products sold online were mislabelled, with only approximately 31% accurately reflecting their declared CBD content. More recent analyses confirm that this problem persists. Saurer and Triemstra [5] tested 202 commercially available CBD products—including tinctures, gummies, vape formulations and topicals—and reported that the majority

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(64.4%) were inaccurately labelled, with heavy metals detected in 44 products, residual solvents in 181 products and pesticides in 30 products, several exceeding regulatory thresholds. Similarly, Spindle et al. [6] reported substantial deviations between labelled and actual cannabinoid concentrations in hemp-derived topical products, with many containing detectable THC despite claims of "THC-free" status.

These are not isolated findings but a reproducible pattern across markets and product categories. Such inconsistencies generate fundamental uncertainty regarding efficacy, safety, dose–response relationships and adverse-event attribution. They also undermine a basic assumption of rational pharmacotherapy: that the prescribed dose reasonably corresponds to the amount of active drug actually administered. A patient or clinician selecting a product based on labelled content may therefore be administering a preparation whose cannabinoid composition differs substantially from that declared.

The Clinical Significance of THC Co-Exposure

The issue is particularly consequential because CBD and Δ^9-tetrahydrocannabinol (THC) possess markedly different pharmacological profiles. CBD is non-intoxicating and has been investigated for anxiolytic, antipsychotic and anticonvulsant effects [1]. THC, by contrast, is a psychoactive cannabinoid acting as a partial agonist at CB_1 receptors and is associated with anxiety, cognitive impairment, psychotomimetic effects and increased risk of psychotic disorders, particularly in vulnerable individuals [7]. Thus, even relatively small amounts of THC may materially alter the neuropsychiatric safety and tolerability profile of a product otherwise perceived as "CBD."

The clinical relevance of THC co-exposure is frequently underestimated. A product containing 100 mg of CBD alongside 5 mg of THC may still be marketed and perceived as a "CBD product." Yet 5 mg of THC represents pharmacologically active exposure and cannot reasonably be regarded as an inert component of a CBD formulation. This distinction becomes even more relevant with repeated administration and in populations particularly susceptible to THC-related adverse effects [7].

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Vulnerable Populations at Risk

This concern is particularly acute in populations especially vulnerable to THC-related adverse outcomes. Children and adolescents represent a salient example. Increasing numbers of cannabis-derived products are being administered to paediatric populations for autism spectrum disorder, behavioural disturbances, anxiety and sleep disorders, among other conditions. Many formulations are not purified CBD but rather full-spectrum or CBD-enriched extracts containing varying concentrations of THC and additional biologically active cannabinoids. This distinction is especially important during neurodevelopment, when the endocannabinoid system participates in synaptic maturation and refinement. Adolescent cannabis exposure has been associated with adverse cognitive and psychiatric outcomes and alterations in brain development [8]. Accordingly, exposing a developing brain to THC cannot be considered pharmacologically equivalent to administering purified CBD.

A growing number of studies in autism spectrum disorder have evaluated cannabis extracts containing both CBD and THC, yet their findings are frequently interpreted and cited as evidence supporting “CBD treatment.” This extrapolation is methodologically problematic: outcomes observed with complex cannabinoid mixtures cannot be attributed to purified cannabidiol in isolation [2]. Persistent failure to distinguish between these interventions generates confusion in the scientific literature and clinical practice and may lead clinicians and patients to extrapolate efficacy and safety data across pharmacologically non-equivalent products.

Individuals with a personal or family history of psychotic disorders constitute another critical population. A substantial body of epidemiological and biological evidence links THC exposure to increased psychosis risk and poorer clinical outcomes [7]. Inadvertent exposure through inadequately characterised CBD products may therefore carry significant consequences for susceptible individuals. For psychiatrists, this is particularly consequential: a product selected partly because CBD is non-intoxicating may inadvertently expose a vulnerable patient to the cannabinoid most strongly associated with psychotomimetic effects and psychosis risk.

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Pregnant and breastfeeding individuals represent an additional group warranting special caution. Cannabis-derived products are increasingly used to manage anxiety, insomnia, nausea and pain during pregnancy despite limited safety data. Volkow et al. [9] documented medical and nonmedical cannabis use among pregnant women in the United States. Fetal and neonatal exposure may involve not only CBD but also THC and other cannabinoids whose developmental effects remain incompletely understood. Product mislabelling and uncertain composition further compound these risks.

Pharmacokinetic Variability Across Routes of Administration

The route of administration introduces another layer of clinically relevant variability. Oils, capsules, oral solutions, edibles, vaporised preparations and sublingual formulations exhibit substantially different pharmacokinetic profiles [2]. Differences in vehicle composition—including carrier oils, emulsifiers and particle size in nanodispersible formulations—may influence cannabinoid absorption and systemic exposure. Consequently, identical nominal doses across products may produce markedly different plasma concentrations and potentially divergent clinical effects. Product heterogeneity therefore extends beyond cannabinoid content: even preparations containing the same nominal amount of CBD cannot automatically be considered pharmacokinetically or clinically interchangeable.

The “Full-Spectrum” Problem

Beyond THC, many extracts contain additional biologically active cannabinoids—including cannabigerol (CBG), cannabinol (CBN), tetrahydrocannabivarin (THCV), cannabichromene (CBC) and their acidic precursors (CBDA, THCA, CBGA)—as well as terpenes, flavonoids and other phytochemicals. Their concentrations may be unstandardised, unreported and variable across commercially available products [2]. Accordingly, “full spectrum” describes neither a standardised pharmacological entity nor an intervention whose effects can automatically be attributed to CBD. Rather than defining composition with the precision expected for a medicine, the term may function primarily as a marketing descriptor.

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Regulatory Implications and a Path Forward

These distinctions converge on a simple but clinically consequential question: when clinicians prescribe CBD and patients take CBD, are they actually using the intervention for which the evidence was generated? The central question is therefore not whether CBD possesses therapeutic potential—the evidence from controlled trials of pharmaceutical-grade CBD is established for specific indications [1,10]—but whether the product being used genuinely corresponds to the cannabidiol evaluated in those trials. It is precisely within this gap between the evidence-generating product and the product reaching the patient that uncertainty regarding efficacy and safety emerges.

The situation is analogous to referring to any morphine-containing preparation as “morphine therapy”—regardless of purity, concentration, accompanying opioids, contaminants, manufacturing standards or route of administration. Such imprecision would be scientifically unacceptable in most areas of medicine. Yet comparable imprecision is increasingly tolerated in the cannabinoid field, facilitated by regulatory fragmentation, commercial pressures and consumer enthusiasm that have outpaced the evidence base. For clinicians, this creates an unusual therapeutic situation in which the name of the purported active ingredient may convey considerably more certainty than the product itself warrants.

As cannabinoid-based therapeutics continue to expand globally, several priorities emerge. Researchers and journal editors should insist on precise characterisation of study interventions, clearly distinguishing purified CBD from CBD-enriched extracts, THC-containing preparations and full-spectrum products [2]. Clinicians should recognise that CBD products are not necessarily pharmacologically equivalent and should counsel patients accordingly, preferably selecting pharmaceutical-grade or otherwise rigorously characterised products with documented composition. Regulators should strengthen quality standards, contaminant testing, accurate labelling requirements and post-marketing surveillance [2–6]. Finally, consensus standards for reporting cannabinoid content, formulation and composition are required so that clinical evidence can be meaningfully compared and translated into practice.

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Ultimately, “CBD” should not be treated as a therapeutic category independent of the product in which it is delivered. Evidence generated with purified, pharmaceutical-grade cannabidiol cannot automatically validate a botanical extract, a full-spectrum preparation or a product with uncertain cannabinoid content simply because its label contains the same three letters. For clinicians, this distinction determines what is actually being prescribed; for patients, what is actually being taken; for researchers, what is actually being tested; and for regulators, what evidence can legitimately support claims of efficacy and safety. When cannabidiol is not cannabidiol, the problem is therefore not merely semantic—it challenges the validity of the entire evidence-to-practice pathway. Cannabinoid-based medicine should ultimately be held to the same pharmacological, clinical and regulatory standards as any other field of therapeutics.

Declaration of Conflicting Interests

JAS Crippa is a co-inventor of patents involving fluorinated CBD compounds (WO/2014/108899; BR1120150164927) and cannabinoid-containing oral pharmaceutical compositions (BR112018005423-2). The University of São Paulo has licensed the former patent to Phytecs Pharm and has an agreement with Prati-Donaduzzi for CBD drug development. He has received consulting and/or speaking fees from BSPG Pharm, PurMed Global, Torrent, Green Care Store, FarmaUSA, Adium, Janssen, Aché, Prati-Donaduzzi, Mantecorp, DSM, Cellera and Ease Labs.

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