JPPT | Review

The Current State of Unapproved Cannabidiol Product Use in Children

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Cannabidiol (CBD) is a naturally occurring cannabinoid isolated from *Cannabis sativa*. CBD has therapeutic benefit for the treatment of seizures associated with various epilepsy syndromes in children; however, data are lacking related to the use of CBD for other indications in pediatric patients. Despite this lack of clinical data, the use of CBD products as a complementary treatment for various conditions in children continues to increase. Thus, it is imperative that those involved in the care of children and adolescents are well informed with current information related to CBD use in pediatrics. This review will address the pharmacology of CBD, legal and regulatory factors, usage patterns, current efficacy data, and safety concerns related to the use of CBD in children and adolescents. Recommendations for clinicians, public health officials, and researchers are also provided to effectively manage the use of unapproved CBD products in the pediatric population.

ABBREVIATIONS ABC-CFXS, Aberrant Behavior Checklist–Community Edition – Fragile X Syndrome; ADHD, attention-deficit hyperactivity disorder; AEA, N-arachidonoylethanolamine; ASD, autism spectrum disorder; AUC, area under the curve; BDNF, brain-derived neurotrophic factor; CBD, cannabidiol; CGI-I, Clinical Global Impression–Improvement; cGMPs, current good manufacturing practices; CNS, central nervous system; DEA, Drug Enforcement Agency; FDA, US Food and Drug Administration; FXS, fragile X syndrome; GABA, gamma–aminobutyric acid; GAD, generalized anxiety disorder; GPR55, G protein–coupled receptor 55; PPARγ, peroxisome proliferator-activated receptor gamma; THC, tetrahydrocannabinol; T_{max}, time to maximal concentration; TRPV, transient receptor potential vanilloid; 5-HT, 5-hydroxytryptamine

KEYWORDS cannabidiol; cannabinoid; pediatrics

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Introduction

Cannabidiol (CBD) use has expanded rapidly in recent decades within the United States, including among children and adolescents.[1,2] It is important for pediatric health care professionals, including pharmacists, to understand key elements related to CBD products to guide conversations with parents and guardians who may be considering or already use such products for the care of their children. This includes the regulatory landscape, clinical science, and safety concerns related to these products.[3–9] Thus, the aims of this review are to provide a comprehensive review of unapproved CBD product use in children and to provide the clinician with practical considerations when communicating with families regarding these products, including the pharmacology, historical and current regulations, safety and efficacy, and health beliefs surrounding use of CBD products.

Pharmacology and Pharmacokinetics of CBD

There are 3 main classes of cannabinoids: endocannabinoids (naturally occurring within the body), phytocannabinoids (naturally occurring within the *Cannabis sativa* plant), and synthetic cannabinoids (synthesized for therapeutic use). Over 100 different phytocannabinoids have been discovered from the *C sativa* plant, with delta-9-tetrahydrocannabinol (THC) and CBD being most abundant.[10] While THC is well known for its psychotropic effects, CBD lacks these properties. In addition, CBD may exert anti-inflammatory, antiemetic, and neuroprotective effects.[11]

CBD is thought to exert its primary action on receptors within the endocannabinoid system. Within this system, 2 endocannabinoids, N-arachidonoylethanolamine (anandamide/AEA) and 2-arachidonoylglycerol, are transferred across the synaptic cleft where they bind to the cannabinoid receptors. The cannabinoid receptors, CB1 and CB2, are inhibitory G protein–coupled receptors. CB1 receptors are the most abundant, with expression on gamma–aminobutyric acid (GABA) and glutamatergic neurons, particularly in areas of the brain associated with motor control, learning, memory, cognition, and emotions. CB2 receptors are less prominent and primarily found in the peripheral tissues including

immune cells, the spleen, and cardiovascular tissues. CB2 is also expressed in neural cells involved in pain perception, located in postsynaptic locations throughout the central nervous system (CNS).[1,10,12,13] Binding of endocannabinoids to CB1 and CB2 receptors results in the release of neurotransmitters such as glutamate, GABA, dopamine, serotonin, and acetylcholine.[1,10,12,13] While human data are limited, the expression of cannabinoid receptors is believed to change throughout development. In rodents, CB1 receptor expression and levels of AEA and 2-arachidonoylglycerol in the CNS peak in adolescence. CB1 receptor expression is thought to peak around 5 years of age in human prefrontal cortex followed by a slow decrease into adulthood.[14] While a full review of these factors is beyond the scope of this review, clinicians should be aware that the clinical effects of cannabinoids may vary throughout development in humans owing to physiologic changes in the endocannabinoid system.

CBD acts as an indirect antagonist of CB1 and CB2 receptors. Compared with THC, which is a strong agonist at CB1 receptors, CBD has a much lower affinity for these receptors, acting as a negative allosteric modulator. Thus, CBD may reduce the clinical effects of THC.[8] CBD is also believed to work by blocking the metabolism and uptake of AEA,[10] allowing for more activation of CB1 and release of downstream neurotransmitters. Further, *in vitro* research suggests that CBD may have CB2 receptor inverse agonism.[15] The interaction of CBD with CB2 receptors expressed in brain circuits that are hyperactive in patients with schizophrenia is also noteworthy.[16] These CB2 receptor interactions likely explain the lack of certain psychotropic effects, such as hallucinations, with CBD compared with THC.

CBD exerts other important effects, such as agonism at glycine, transient receptor potential vanilloid (TRPV)-1, 5-hydroxytryptamine (5-HT) 1A, and 5-HT3A receptors; partial agonism at D2 and D3 receptors; inhibition at sodium and calcium channels; modulation of peroxisome proliferator-activated receptor gamma (PPARγ); and antagonism at G protein–coupled receptor 55 (GPR55).[8,10] The anticonvulsant properties of CBD are thought to be mediated by interaction with many of these receptors, including GABA, glycine, TRPV1, TRPV2, and GPR55 receptors.[8] Additionally, the administration of CBD increases brain-derived neurotrophic factor (BDNF) and 5-HT levels in animal models. Considering decreased BDNF levels in the CNS in patients with depression, the potential to modulate 5-HT1A and 5-HT3A receptors, and interactions with PPARγ and other PPARs, CBD may have antidepressant and anxiolytic effects.[8] This also points to the potential for CBD to be used in the treatment of substance use and dependence.

Most of what is known regarding the pharmacokinetics of CBD is derived from studies of oil-based oral formulations used for the treatment of seizures associated with epilepsy. The oral bioavailability of CBD is relatively low at 13% to 19% owing to variable absorption and extensive first-pass metabolism via CYP3A4.[17] Absorption after oral administration is greatly increased when CBD is given with a high-fat meal, demonstrated by a 5-fold increase in maximum concentration and a 4-fold increase in area under the curve (AUC). Additionally, the AUC of CBD after oral administration is dose-dependent.[18] Time to maximal concentration (T_{max}) after administration of oromucosal drops or sprays ranges from 1.64 to 4.2 hours, with similar T_{max} values reported with sublingual drops. The bioavailability of CBD after smoking or inhalation has been reported to be around 31%.[17] Absorption and systemic exposure of CBD after topical administration is highly variable because of lipophilic properties and a tendency to degrade when exposed to light, temperature, and air.[19]

CBD is highly protein bound (>94%), leading to a large volume of distribution (20,963 to 42,849 L in adults).[4] The major CYP450 enzymes responsible for the biotransformation of CBD to its active metabolites are CYP3A4 and CYP2C19.[20] CYP2C9, CYP2C19, UGT1A9, and UGT2B7 have also been implicated in the metabolism of CBD. The resultant half-life of CBD in children is highly variable, ranging from 1 to 2 days with chronic oral administration, and may be significantly shorter with other routes of administration.[17] Nearly 40 different metabolites of CBD have been identified, all with varying potency.[21,22] 7-Hydroxy CBD, the primary active metabolite of CBD, has reduced activity compared with CBD itself and exhibits unique pharmacokinetic properties.[20] For example, the AUC of 7-hydroxy CBD is 38% lower than CBD itself.[4] CBD is primarily excreted in the feces.[4] While a full review of the pharmacology and pharmacokinetics of CBD is beyond the scope of this review, clinicians should be aware of how these factors affect the clinical effects of CBD in children.[23]

Factors Affecting Unapproved CBD Product Use in the United States

In 2018, the first CBD (Epidiolex, Greenwich Biosciences, Carlsbad, CA) dosage form was approved by the US Food and Drug Administration (FDA).[3] Epidiolex is an oil-based oral solution containing 100 mg/mL of CBD and is indicated for the treatment of seizures associated with Dravet syndrome, Lennox-Gastaut syndrome, and tuberous sclerosis complex.[4] While the use of Epidiolex in children with various epilepsy diagnoses continues to grow, so does the use of unapproved CBD products for epilepsy and other indications. CBD products have reportedly been used in a variety of other disease states as both monotherapy and adjunctive therapy,[5–7] including the treatment of muscle spasticity, sleep disorders, loss of appetite, nausea and vomiting, and neuropsychiatric disorders including autism spectrum disorder (ASD).[8,9] Notably, all other CBD-containing

products are not approved by the FDA and are thus considered unapproved products.

The history of CBD use and approval within the United States is summarized in Figure 1.[2,24–29] Prior to 2018, legal access to CBD products was limited.[2,24–29] However, since the Farm Bill in 2018, there has been increasing legal access to a broad variety of CBD products.[24–28] Recent growth in CBD use is influenced by the changing public perceptions surrounding its utility for a wide range of indications and acceptability for use.[24]

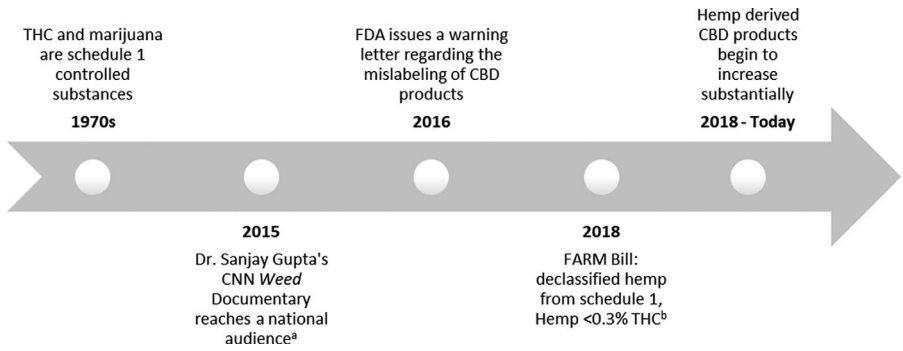
Analysts estimate that the CBD market could grow from an estimated $4.9 to $12.8 billion in 2021 to $47.2 to $56.2 billion by 2028.[24,30] Increased consumer interest and subsequent awareness in this market have spurred growth, and companies continue to expand research efforts to demonstrate the efficacy of CBD products in a broad variety of disease states and conditions.[31,32] Growth is also due to the broadening of available products in recent years, which now include oils, gummies, tinctures, infused food products, skincare products, sprays, patches, vape pens, and more.[24]

Changing attitudes toward CBD and prescription pharmaceuticals have also contributed to the increasing CBD market. Parents are often looking for alternative "natural" treatments for children. Because the general public is aware that CBD products are derived from a plant source, many parents may believe that these offer a natural and safer alternative to FDA-approved pharmaceuticals. This has driven research into public perceptions of CBD.[31,32] Perceptions of other drugs, such as opioids, have also changed parental attitudes toward CBD. For decades, opioids have been a therapeutic mainstay of pain management. However, there have been significant challenges with opioids involving misuse and addiction.[24] The visibility of the opioid epidemic and public media portrayal of its effects have resulted in many patients and families seeking alternative remedies for managing pain, including CBD products.[32]

Unapproved CBD products are purchased from both offline and online distributors. However, owing to a decrease in consumer confidence surrounding e-commerce with CBD products, the offline distribution is expected to make up an increasingly larger percentage of the market.[24] While dispensaries are responsible for most CBD sales today, predictions show a shift away from dispensaries toward retail stores, including some pharmacies in states that allow this practice.[24] With prices often ranging from $60 to $70 per unit (i.e., 1–fl oz bottle of oil, 30-day supply of gummies, 1.7–4 fl oz bottle or jar of topical cream/lotion), CBD products can have a substantial impact on community pharmacy profits owing to the margin on the products.[28] However, CBD products can also have a substantial negative impact on patient health care costs, as patients may purchase multiple products monthly, depending on the dose required to treat the condition. Health savings accounts and flexible spending accounts cannot be used to pay for CBD products, either. It is important to consider this impact, particularly for families that struggle with elements of the social determinants of health, such as financial stability or health insurance.

While the growth of the CBD market appears to be exponential, significant concerns remain related to mislabeling and illegal marketing. As noted by the FDA, "marketing unapproved products, with uncertain

Figure 1. Timeline of key events in CBD use and legality in the United States.



CBD, cannabidiol; CNN, Cable News Network; FARM Bill, Federal Agriculture Improvement Act of 2018; FDA, US Food and Drug Administration; THC, tetrahydrocannabinol.

[a] In 2015, Weed, the influential documentary highlighting Charlotte Figi's story was aired on CNN. This documentary showcased Charlotte's story of epilepsy and her positive experience with CBD products. It also elaborated on some of Colorado's biggest medical marijuana growers, the Stanley brothers, and their branding of Charlotte's Web hemp oils in 2012.

[b] This law, for the most part, leaves regulation regarding hemp production and marketing up to the states. The United States is thought to be one of the largest consumers of CBD-derived products. This is perceived to be largely due to the Farm Bill of 2018.

dosages and formulations can keep patients from accessing appropriate, recognized therapies to treat serious and even fatal diseases."[3] With expanding growth of the CBD market, it is important to monitor and address unreliable safety and efficacy data. Changing regulatory guidelines and expanded guidance may provide enhanced information regarding safety and efficacy, while preventing mislabeling and illegal marketing.[33]

Regulatory and Legal Landscape of Unapproved CBD Products

The regulatory and legal landscape of CBD products continues to change. Most updates to CBD regulations have occurred rather slowly, but the future of these standards is likely to change much more rapidly as states start to play a larger role in deciding how CBD and other hemp-derived products are managed.

Federal Regulations. Prior to 2018, all CBD-containing products were considered Schedule I controlled substances by the Drug Enforcement Agency (DEA). The 2018 Farm Bill created distinctions between cannabis (e.g., marijuana), which was illegal to cultivate, and hemp, which was distinguished as a legal crop if it contained less than 0.3% THC by weight.[34] Six months later, the FDA approved the first prescription form of cannabidiol, branded as Epidiolex.[3] According to the Food, Drug, and Cosmetic Act, supplements and foods cannot contain drugs, and any supplements or foods that do contain active drugs cannot be shipped across state lines.[35] These stipulations mean that any product other than Epidiolex does not meet FDA approval requirements as a drug or dietary supplement. Given the variety of both foods and supplements containing CBD, there are significant concerns whether CBD products fit within legal distribution regulations. Though many of these products are prohibited by the letter of the law, the current regulatory pathways through the FDA are insufficient to provide to fully manage the desire for CBD products and the corresponding risks associated with their use.[36] Owing to limited centralized regulation, as well as the Farm Bill's federal decriminalization of hemp cultivation, states typically determine the legality of CBD products, making the distribution and marketing of CBD products within states and across state lines increasingly complicated.

It is important to note that all manufacturers are still required to follow the current good manufacturing practices (cGMPs) for dietary supplements as specified in Title 21 of the Code of Federal Regulations.[37] Many dietary supplements and food additives containing CBD have remained on the market following this legislation, and there are concerns that they do not follow cGMPs. Further, citing the lack of data regarding long-term use and a lack of consistency with self-administered doses, the FDA has indicated that new regulations need to be established that will likely be stricter on current development of CBD supplements.[36] Additionally, the DEA has recently recommended that marijuana be reclassified as a Schedule III controlled substance following the recommendation of the Health and Human Services Department. Even if these regulatory changes are made, it is uncertain whether new rules and regulations will be enforced properly. As the FDA and the DEA work with lawmakers to develop clearer regulations, states will have to decide the processes and allowances for CBD sales, considering future federal regulations.

State Regulations. While several states have allowed expanded access to unapproved CBD products, a majority have instituted certain conditions that limit either how CBD can be supplied or from where it can be sourced. Specifically, most of the states that have restrictions regarding the supply of CBD either limit the THC content, require CBD to be derived from hemp, require medical cannabis licensures for products with higher THC content, or limit the dosage forms (e.g., edibles) that can be dispensed or sold. Further categorical information on state regulations can be found in Table 1.[38] For example, California has recently prohibited hemp-derived THC products and raised the minimum age to purchase hemp products to age 21 years. Both medicinal and recreational CBD

Table 1. State Regulations Regarding CBD Products as of July 2024

Fully Legal	Conditionally Legal	
Alaska	Alabama	New Mexico
Arizona	Arkansas	North Carolina
California	Delaware	North Dakota
Colorado	Florida	Ohio
Connecticut	Georgia	Oklahoma
District of Columbia	Hawaii	Pennsylvania
Illinois	Idaho	Rhode Island
Maine	Indiana	South Carolina
Massachusetts	Iowa	South Dakota
Michigan	Kansas	Tennessee
Montana	Kentucky	Texas
Nevada	Louisiana	Utah
New Jersey	Maryland	West Virginia
New York	Minnesota	Wisconsin
Oregon	Mississippi	Wyoming
Vermont	Missouri	
Virginia	Nebraska	
Washington	New Hampshire	

are allowed.[39] Georgia has banned the sale of all CBD products to persons younger than 21 years beginning October 1, 2024, but does not have the stricter prohibitions on hemp-derived products.[40]

Product Quality Assurance. As noted earlier, the FDA is considering new regulations related to CBD products,[36] while reaffirming their stance that unapproved CBD products do not meet the requirements necessary to be categorized as dietary supplements nor have any been evaluated for approval as a drug. Despite lacking an appropriate regulatory pathway for these products, CBD products are expected to be produced according to the good manufacturing requirements for both drugs and dietary supplements, including assessing purity, strength, and composition.[37] Yet, numerous reports suggest that CBD products continue to suffer from issues with label accuracy, including both incorrect concentrations and composition.

Spindle et al[41] reported that of the 105 products tested, only 24% were accurately labeled for their CBD content, while only 38% were correctly labeled for THC content. Similarly, the FDA conducted a sampling study of CBD and THC levels in 2020 to determine if the tested product ingredient concentrations were within 20% allowable deviation from the label.[42] They found that only 35% of products tested contained CBD levels within 20% of the label claim.[42] Suppliers of these CBD products are not required to report inactive ingredients, the CBD source, or whether pesticides or other chemicals were used in the growing or production process. This is an important area of consideration for health care professionals when counseling families on the safe use of CBD products.

Parental Health Beliefs and CBD Use Patterns Among Children

Despite limited information available on use patterns, there is a general understanding that parents have increasingly used unapproved CBD products for their children. A recent nationally representative US survey of parents found that nearly one-third (31.3%) reported that they had administered an unapproved CBD product to their child who was diagnosed with attention-deficit/hyperactivity disorder (ADHD), ASD, and/or generalized anxiety disorder (GAD).[43] Usage varied depending on geographic region, which could be due to state laws and regional societal views regarding CBD products. The highest prevalence was found in the western region at 43.4%, and the lowest was found in the northeastern region at 18.6% ($p < 0.05$).[43]

Many different formulations of unapproved CBD products are available, some of which mimic candies, which could increase the risk of accidental overdose in children. In one study, the most common CBD dosage form administered to children by parents was edible gummies. Oils, drops, tinctures, topical creams and lotions, lollipops, and other edibles were also reportedly administered to children.[43] Perceptions of CBD products overall vary. Most consumers desire well-known or trusted companies to produce CBD products, owing to a higher likelihood of safety controls in place, higher manufacturing standards, and more experience in producing high-quality products consistently.[44] Survey findings also indicate that over two-thirds of consumers who have never purchased CBD products are more likely to purchase them if they are regulated by a federal agency.[44] When asking parents, 83% prefer FDA regulation of CBD products, with 74% preferring it to be prescribed only.[45] While increased regulation may result in increased perceived safety and higher use of CBD products, it could raise the cost of manufacturing CBD products,[33] driving the consumer costs even higher. It may further increase use of unapproved products as well in an effort to reduce out-of-pocket costs.

Parents have used or contemplated the use of CBD products for a broad variety of indications. These include common uses in epilepsy[46] as well as emerging therapeutic areas such as neurologic and psychiatric disorders (GAD, ADHD, ASD),[43] juvenile rheumatoid arthritis,[47] and fragile X syndrome (FXS).[48] Expanding use indicates positive perceptions of CBD product efficacy and safety along with high interest for use. Interestingly, in a representative survey of parents who give their children CBD products for ASD, GAD, and/or ADHD, parents perceived stronger community support surrounding CBD use.[43] There is even less information on pediatric patients' perceptions of CBD products, but one study evaluated CBD oil use by adolescents in inflammatory bowel disease and found they had positive perceptions of efficacy.[49]

Effectiveness of CBD Products in the Pediatric Population

The efficacy of Epidiolex for the treatment of seizures in children associated with Lennox-Gastaut syndrome, Dravet syndrome, and tuberous sclerosis complex has been established through multiple prospective, placebo-controlled trials.[5,50] However, research efforts regarding the efficacy of Epidiolex in other forms of epilepsy remains ongoing. Further, data evaluating the use of unapproved products in children for indications other than epilepsy require additional scrutiny. Thus, we performed a rapid review of CBD studies in the pediatric population for indications other than epilepsy, published through 2022, using MeSH terms in PubMed with the aid of a research librarian. The articles were then screened in Covidence with the following inclusion criteria: research study (controlled study, case report, case series); uses purified, unapproved CBD products (contains <0.3% THC); and contains data on patients 0 to 21 years of age. Articles were excluded if they included Epidiolex, medical marijuana, or treated epilepsy. Two researchers independently reviewed each article for inclusion and exclusion, with a third

researcher resolving conflicts. The first phase of review focused on titles and abstracts, and the second phase of review focused on full text. A total of 576 studies were imported into Covidence, with 203 duplicates removed. After the review phases, a total of 14 studies were included. Table 2 summarizes these publications evaluating the efficacy and safety of CBD in children and adolescents.

Briefly, our review generated 14 studies that included 5 randomized controlled trials, 4 case reports/series, and 3 open-label studies (typically linked to a drug study phase [I, II, or III]). The most common condition was ASD (n = 5), followed by FXS (n = 2). Two studies were broad and included multiple diseases or conditions. Efficacy and safety results varied among the studies. Data from the studies are discussed further below.

Within the published literature, the use of CBD for the treatment of core deficits and maladaptive behaviors associated with ASD has received the most attention. To date, only aripiprazole and risperidone have been approved by the FDA for the treatment of irritability and aggression associated with ASD, and no medications lead to improvement in the core deficits associated with ASD.[51] These realities have been a primary driver of research to elucidate whether CBD might be efficacious for children with ASD. The largest of these trials was a prospective, double-blind, placebo-controlled crossover study published in 2021.[52] The investigators enrolled 150 participants 5 to 21 years of age with ASD. Participants were randomly assigned in a 1:1:1 fashion to receive either placebo, a whole-cannabis plant extract containing a 20:1 ratio of CBD to THC, or a purified CBD product containing the same 20:1 ratio of CBD to THC for 12 weeks. The whole-cannabis plant extract product retained all natural cannabinoids and plant terpenes, while the purified product did not. After a 4-week washout period, participants were switched from the placebo arm to a treatment arm or vice versa. Participants were started on 1 mg/kg/day of CBD and doses were increased by 1 mg/kg/day every other day to a maximum of 10 mg/kg/day for patients weighing between 20 and 40 kg or 7.5 mg/kg/day in patients >40 kg. No significant differences in Home Situation Questionnaire–ASD scores were observed when the CBD-rich products were compared with placebo. When comparing, Clinical Global Impression–Improvement (CGI-I) scale, 49% of patients receiving the whole plant extract, 38% receiving the purified CBD-rich product, and 21% receiving placebo reported improvement. Only the difference in CGI-I between the whole plant extract and placebo was statistically significant ($p = 0.005$). Median improvement in Social Responsiveness Scale-2 scores were 3.6 points for placebo, 14.9 points for whole plant extract ($p = 0.009$), and 8.2 for the purified product ($p = 0.80$). This secondary outcome is important to note because it may signal an improvement in social communication, one of the core deficits seen in patients with ASD. Over 20% of the participants reported somnolence and decreased appetite when taking either the whole plant extract or purified product. No serious adverse events were reported.[52]

Other studies have also evaluated the use of CBD in ASD. Barchel et al[53] evaluated 53 children between the ages of 4 and 22 years to receive a cannabis oil containing a 20:1 ratio of CBD to THC. The recommended dose of CBD was 16 mg/kg/day up to a maximum of 600 mg/day. Overall improvement in symptoms related to ASD was reported by 74.5% of parents. Looking at specific symptoms, 26 of 38 (68.4%) parents reported an improvement in hyperactivity, 23 of 34 (67.6%) reported an improvement in self-injury, 15 of 21 (71.4%) reported an improvement in sleep, and 8 of 17 (47.1%) reported an improvement in anxiety. However, none of these improvements were considered statistically significant when compared with conventional treatment responses published in the literature.[53] Somnolence and changes in appetite were the most reported adverse effects. However, this trial is limited by the small sample size, lack of blinding, lack of a true comparator group, and a requirement of only 30 days of follow-up.

Preliminary data on the use of CBD-rich products for the treatment of complex motor disorders with predominant spasticity or dystonia are promising. Libzon et al[54] conducted a pilot study in which pediatric participants between the ages of 1 and 17 years were given 5% CBD-enriched oil with either 0.25% or 0.83% THC for a duration of 5 months. These products had CBD to THC ratios of 20:1 and 6:1, respectively. The study was conducted in Israel, where fewer regulatory constraints allowed for the higher concentration of THC to be used. Patients were administered 1 drop 3 times daily of the allocated oil, with the dose titrated up until the drug was unable to be tolerated, serious side effects were noted, or a maximum of 15 mg/day of THC was reached. Twenty participants completed the study. The mean CBD doses at the final study visit were 3.73 mg/kg/day in the 6:1 group and 5.53 mg/kg/day in the 20:1 group ($p = 0.42$). Statistically significant improvements for the total cohort were seen in numerical rating of dystonia, spasticity, mood, stool function, sleep, pain, and appetite. Additionally, improvements were seen in both the Gross Motor Function Measure and the Cerebral Palsy Child questionnaire for quality of life. Statistically significant differences in clinical effects between the 2 products were not observed owing to the small sample size of the study. Worsening of seizures was reported in 2 patients, including one that experienced new onset gelastic seizures. One patient experienced excitation with rapid dose titration, and one reported mood fluctuations with concurrent methylphenidate use.[54]

Interest in using CBD in children with intellectual disability is also growing. Efron et al[55] published a

Table 2. Efficacy and Safety of CBD Products in Children and Adolescents for Treatment of Conditions Other than Epilepsy

Author (Year) | Study Design	CBD Product(s)	Condition(s) and Population	Outcomes
Aran[52] (2021) | RCT	167 mg/mL CBD and 8.35 mg/mL THC CBD:THC ratio 20:1	ASD 150 participants 5–21 years of age	**Efficacy:** *No difference between groups (CBD vs placebo):* • Home Situation Questionnaire–ASD • Autism Parenting Stress Index *Significant improvement for CBD vs placebo in:* • CGI-I scale with disruptive behavior anchor points (p = 0.005) • Social Responsiveness Scale (p = 0.009) **Safety:** • Somnolence was more common in CBD vs placebo (p < 0.001) • No other significant differences or severe/serious adverse events
Barchel[53] (2018) | retrospective observational study	Concentration of 30% and a CBD:THC ratio 20:1 Dosed by weight: • CBD - 16 mg/kg, up to 600 mg daily • THC - 0.8 mg/kg, up to 40 mg daily	ASD 53 participants 4–22 years of age	**Efficacy:** Change in symptoms: • No change = 21.6% • Improvement = 74.5% • Worsening = 3.9% **Safety:** Most common adverse event – somnolence
Berry-Kravis[58] (2022) | RCT	Transdermal gel (4.2% w/w CBD concentration) dosed by weight: • ≤35 kg = 250 mg daily • >35 kg = 500 mg daily	Fragile X syndrome 212 participants 3–17 years of age	**Efficacy:** *Improvement but no significant difference:* • Social avoidance • Irritability • Unresponsiveness/lethargy *Patients with ≥90% methylation of FMR1:* • Significant improvements in unresponsiveness/lethargy (p = 0.020) • Significant improvements in Caregiver Global Impression: SA and isolation, irritable and disruptive behaviors, and social interactions (p = 0.038, p = 0.028, and p = 0.002, respectively) **Safety:** Most common adverse effect was upper respiratory tract infection (double occurrence vs placebo)
Chelliah[59] (2018) | case series	Various CBD dosage forms including spray, oil, and cream	Epidermolysis bullosa 3 cases 6 months, 3 years, and 10 years of age	**Efficacy:** Improvement of blistering and symptoms associated with epidermolysis bullosa

(Table cont. on page 571)

Table 2. Efficacy and Safety of CBD Products in Children and Adolescents for Treatment of Conditions Other than Epilepsy *(cont.)*

Author (Year) | Study Design	CBD Product(s)	Condition(s) and Population	Outcomes
Efron[55] (2021) | RCT	98% CBD in oil, dosed by weight: • 5 mg/kg/day, titrated up to a maintenance dose of 20 mg/kg/day	Intellectual disability and severe behavioral problems 8 participants 8–16 years of age	**Efficacy:** • Significant reduction in Aberrant Behavior Checklist-Irritability subscale symptoms in the CBD group. ($p < 0.05$) • No significant reduction in the placebo group. **Safety:** No dose reductions, well tolerated
Heussler[57] (2019) | phase 1/2 open-label	Transdermal CBD, up to 250 mg daily	Fragile X syndrome 20 participants 6–17 years of age	**Efficacy:** Statistically significant reduction: • Mean Anxiety, Depression, and Mood Scale score ($p < 0.001$) • Manic/hyperactive behavior ($p < 0.001$) • Social avoidance ($p < 0.001$) • Compulsive behaviors ($p = 0.03$) • Secondary outcomes: Aberrant Behavior Checklist–Community, pediatric anxiety rating scale, pediatric QOL inventory, visual analogue scale (hyperactivity/impulsivity, tantrum/mood, and anxiety) **Safety:** • No serious adverse events • >10% experienced gastroenteritis, vomiting, and upper respiratory tract infection
Koren[56] (2021) | case report	CBD oil, smoked, and flower	Disruptive symptoms related to FASD 2 cases 5 and 12 years of age	**Efficacy:** Improvement in disruptive symptoms • Significant decrease in disruptive behavior score ($p = 0.0002$) across all 5 cases **Safety:** No reports of serious adverse drug reactions
Libzon[54] (2018) | RCT	5% oil formulation • 0.25% δ-9-tetrahydrocannabinol (THC) 20:1 • 0.83% THC 6:1 group	Complex motor disorders 20 participants 1–17 years of age	**Efficacy:** Significant improvement across multiple efficacy assessments • Barry-Albright Dystonia: $p = 0.009$ • Numeric Rating Scale for spasticity and dystonia: $p = 0.002$ • Gross motor function: total and lay, $p = 0.001$; sit, $p = 0.009$ • Quality of life: $p = 0.036$ • Visual Analog Scale: $p = 0.022$
Madden[81] (2020) | case study	CBD oil, up to 50 mg, 6 times per day	Neuroendocrine tumor with metastatic disease 13 years of age	**Safety:** Potential drug interaction between methadone and CBD, leading to fatigue and sleeplessness

(Table cont. on page 572)

Table 2. Efficacy and Safety of CBD Products in Children and Adolescents for Treatment of Conditions Other than Epilepsy *(cont.)*

Author (Year) | Study Design	CBD Product(s)	Condition(s) and Population	Outcomes
Palumbo[82] (2022) | phase 2 open-label	Transdermal CBD, 250 or 500 mg/day	ASD 37 participants 3–17 years of age	**Efficacy:** Statistically significant improvement: $p < 0.05$ • All Aberrant Behavior Checklist–Community subscales • Parent-Rated Anxiety Scale–ASD score • Autism Parenting Stress Index • Each Autism Impact Measure domain • Irritability **Safety:** • No serious adverse effects • One discontinuation due to local site reaction • No changes in laboratory parameters or ECG
Perez-Vilar[60] (2023) | case series	CBD (unspecified)	6496 cases All ages	**Safety:** Derived from American Association of Poison Control Centers reports • Cases most common in children 2–12 years of age due to unintentional exposure • Most frequent clinical effects: CNS depression, tachycardia, vomiting, neurological, dizziness/vertigo, nausea, and agitation • Most outcomes were mild in nature, with only 1 death likely due to comorbid conditions
Silva[83] (2022) | RCT	0.5% (5 mg/mL) CBD:THC ratio 9:1	ASD 64 participants 5–11 years of age	**Efficacy:** *Significant improvements in CBD vs placebo:* • Psychomotor agitation ($p < 0.01$) • Number of meals per day ($p < 0.05$) • Social interaction ($p < 0.001$) • Anxiety ($p < 0.05$) *No improvements in:* • Aggression, concentration, sleep, speech, stereotypy • Autism Treatment Evaluation Checklist • Childhood Autism Rating Scale **Safety:** 10% with dizziness, insomnia, colic, and weight gain
Stolar[84] (2022) | prospective, single arm, ongoing, open-label phase III study	CBD oil CBD:THC ratio 20:1	ASD 59 participants 5–25 years of age	**Safety:** Significantly higher after therapy: • LDH ($p = 0.003$) • Free T4 ($p = 0.03$) • TSH ($p = 0.01$)

(Table cont. on page 573)

Table 2. Efficacy and Safety of CBD Products in Children and Adolescents for Treatment of Conditions Other than Epilepsy *(cont.)*

Author (Year) | Study Design	CBD Product(s)	Condition(s) and Population	Outcomes
Zürcher[85] (2022) | retrospective, observational	THC/CBD THC Pure CBD solutions with concentrations of 2.5%, 5%, and 10% contained 0.7 mg, 1.4 mg, and 2.8 mg per drop	Various 51 participants in CBD group 4–17 years of age	**Efficacy:** • 33 of 51 experienced treatment success with the CBD • Mostly used to treat pain, seizures, and sleep disorders • Largest treatment effects were reported for pain, spasticity, and frequency of seizure in participants treated with THC, and for those treated with CBD only, the frequency of seizures **Safety:** • Tiredness, sedation, and dry mouth

ASD, autism spectrum disorder; CBD, cannabidiol; CGI-I, Clinical Global Impression–Improvement; CNS, central nervous system; ECG, electrocardiogram; FASD, fetal alcohol spectrum disorder; LDH, lactate dehydrogenase; QOL, quality of life; RCT, randomized controlled trial; SA, Static Assessment; THC; tetrahydrocannabinol; TSH; thyroid-stimulating hormone; T4, thyroxine

problems in children 8 to 16 years of age, diagnosed with intellectual disability and severe behavioral problems. Eight participants were allocated to receive 98% CBD oil or placebo for a total of 8 weeks. An initial dose of 5 mg/kg/day in divided doses was then titrated by 5 mg/kg/day every 3 days to a maintenance dose of 20 mg/kg/day with a total daily maximum dose of 500 mg. While the authors reported favorable efficacy data related to behavioral concerns, conclusions regarding the utility of CBD in these children cannot be made owing to the trial design and the resulting small sample size.[55]

Several case reports have been published regarding the use of CBD in children with other congenital disorders. Koren et al[56] describe the use of cannabis in 2 children and 3 young adults diagnosed with fetal alcohol spectrum disorder. The first of these children was a 5-year-old male also diagnosed with ADHD, global cognitive delay, and conduct disorder. The patient received 2 drops of a 20% CBD oil that also contained 0.2% THC. An improvement in the frequency of tantrums and aggression was reported along with an improvement in social communication. The second child was a 12-year-old male with comorbid learning disability and conduct disorder. This patient received 3 drops of an oil containing 15% CBD and 1% THC. Improvements in aggression, restlessness, and impulsivity were reported. It is important to note the drastic reports of symptom improvement despite very small doses of CBD in these 2 children. The remaining reports in 3 young adults involved inhalation or ingestion of cannabis preparations from the whole plant instead of CBD-specific products. No patients experienced adverse effects.[56]

Fragile X syndrome has been associated with signaling changes in the endocannabinoid system. An early phase 1/2 open-label study found improvements in behavioral outcomes with no serious adverse events. However, >10% of patients did experience gastrointestinal issues as well as upper respiratory tract infections.[57] Thus, Berry-Kravis et al[58] conducted the CONNECT-FX trial, a phase 3, double-blind, placebo-controlled trial of ZYN002, a novel transdermal CBD 4.2% gel in patients 3 to 17 years of age with FXS. Participants were randomly assigned to receive ZYN002 or placebo for 12 weeks. The dose of CBD was 250 mg/day in divided doses for patients ≤35 kg in weight, and 500 mg/day for patients >35 kg. The mean age of the 212 patients enrolled was 9.7 years. No statistically significant differences were observed for the primary outcome of change in social avoidance as measured using the Aberrant Behavior Checklist–Community Edition FXS (ABC-C_{FXS}) social avoidance subscale when the total cohort was evaluated. However, in the patients with ≥90% methylation of *FMR1* gene, differences were observed in ABC-C_{FXS} social avoidance subscale, Caregiver Global Impression–Change in social avoidance and isolation, irritability, and disruptive behaviors. Patients with ≥90% methylation of *FMR1* gene accounted for 79.7% of patients enrolled. The most common adverse effect reported was pain at the application site. No serious adverse events were reported in this study.[58]

Case reports have been published on the use of other topical CBD preparations in children for the treatment of epidermolysis bullosa, a group of congenital dermatoses that lead to bullae, blisters, and scarring of the skin and mucous membranes.[59] A 6-month-old male with recessive dystrophic epidermolysis bullosa was initiated on a CBD spray by the parents. This was misted over the affected areas 2 or 3 times daily. The parents reported a reduction of blistering, faster healing

of chronic wounds, and discontinuation of morphine prior to dressing changes. The second case involved a 4-year-old female with epidermolysis bullosa and *KRT5* mutation who was administered a blend of emu and CBD oils twice daily. Per parent report, healing time of facial blisters was reduced by 50%, the number of blisters was reduced, and the patient experienced reduced pain with ambulation. Lastly, a 10-year-old boy with debilitating keratoderma requiring wheelchair assistance was initiated on a topical CBD oil and cream. The family reported a reduction in blistering, reduced wheelchair use, and improved ambulation. Notably, the patient was able to discontinue regular use of naproxen and gabapentin for pain management following the use of topical CBD. Additional details about the specific CBD products used were not reported.[59] While controlled clinical trials are necessary to determine whether CBD is truly efficacious for this indication, the potential anti-inflammatory and analgesic properties may explain these findings.

While literature regarding the efficacy of unapproved CBD products in the treatment of various conditions in children and adolescents continues to grow, many publications are fraught with concerns, including small sample sizes, lack of methodologic rigor, variance in products used, a wide range of dosing strategies, short duration of follow-up, and positive publication bias. Interestingly, there are no published reports on the efficacy of CBD in children and adolescents with ADHD or GAD despite recent reports of use for these indications.[43]

Safety Concerns Related to Unapproved CBD Products

Poison centers in the United States began to see an increase in calls related to CBD in 2014; between July 2014 and June 2021, the US National Poison Data System reported 6496 cases involving CBD products, with 85.2% involving exposure to unapproved CBD products.[60] Children and adolescents younger than 18 years accounted for 51.2% of all cases.[60] Exposure to other products was observed in 19.1% of cases, and 18 cases required admission to a critical care unit. The most common clinical effects were CNS depression, tachycardia, and vomiting. Other effects reported include ventricular arrhythmias, non–ST elevation myocardial infarction, myopericarditis, bradycardia with heart block, blood pressure changes, respiratory depression, dyspnea, hallucinations, and contact dermatitis. It should be noted that the purity of these products was unknown; thus, these effects may be attributed to other substances also contained in the CBD products or coadministered substances.[60]

Adverse effect reporting in studies evaluating unapproved CBD products is variable and difficult to evaluate based on the varying doses and product formulations, as well as often being coadministered with other drugs. Based on clinical trials involving Epidiolex, several adverse effects are specifically associated with systemic CBD exposure. The most common dose-related adverse effects include somnolence. Diarrhea is often observed with increasing doses, possibly related to the amount of oil administered as CBD dosages are increased. Cannabinoid hyperemesis syndrome has not been reported in patients taking purified CBD products.[4] However, this may occur with unapproved CBD products because these often contain varying mixtures of cannabinoids. Thus, clinicians should maintain a healthy suspicion for cannabinoid hyperemesis syndrome in patients who are receiving an unapproved CBD product and present with abdominal pain, early morning nausea, loss of appetite, intractable cyclic nausea and vomiting, or using hot showers to provide temporary symptom relief.[61] This syndrome typically does not respond to antiemetic therapy and resolves with cessation of the marijuana-derived product.[61]

Additional studies evaluating the clinical toxicity of CBD indicate that doses of 20 mg/kg/day or higher are sufficient to produce a variety of adverse effects, including somnolence, decreased appetite, diarrhea, and increases in serum transaminases.[62,63] Patients who are treated with CBD for long periods often experience weight loss and/or loss of appetite, leading to growth issues. In addition, many studies report moderate to severe increases in aspartate aminotransferase, alanine aminotransferase, and, to a lesser extent, gamma-glutamyl transferase. However, these results are confounded by the higher doses used and the coadministration of other antiseizure medications. The risk of transaminase elevations is most common in the first 2 months of therapy when used in children with epilepsy, and the risk increases significantly with concomitant administration of valproic acid, and to a lesser extent, clobazam.[4] It is noteworthy that nonclinical studies in rhesus monkeys have demonstrated increases in liver weight, which suggests that CBD may directly cause hepatotoxicity.[63,64]

Owing to metabolism via hepatic enzymes and other effects on drug metabolism, the risk of drug-drug interactions with CBD is high when used systemically. CYP3A4, CYP2C19, CYP2C9, CYP2C19, UGT1A9, and UGT2B7 are all important in the metabolism of CBD.[20] From a clinical perspective, CBD doses may need to be increased when administered with carbamazepine, oxcarbazepine, phenobarbital, or phenytoin owing to enzyme induction. CBD is also an inhibitor of CYP1A2, CYP2B6, CYP2C8, CYP2C9, CYP2C19, CYP2D6, and UGT2B7.[65,66] Concomitant use of CBD with clobazam leads to the accumulation of N-desmethylclobazam, a potent active metabolite of the parent drug. Some clinicians recommend empirically reducing the clobazam dose by up to 50% when initiating concomitant CBD. Close monitoring and careful titration of clobazam doses is necessary with this combination. CBD is also

known to alter the metabolism of certain antipsychotics, selective serotonin reuptake inhibitors, tricyclic antidepressants, and opioids. CBD can inhibit the metabolism of certain proton pump inhibitors, such as omeprazole, which is commonly used in children.[65,66] Additionally, oral doses of CBD should be reduced in patients with hepatic impairment.[4]

Purified forms of CBD could be safer for patients instead of the unapproved CBD products that oftentimes yield unpredictable proportions of THC. For example, a *post hoc* analysis of a phase 3 safety study assessing the safety of diazepam nasal spray in patients who also received CBD treatment found that the lowest rates of treatment emergent adverse events attributed to diazepam were reported in patients who received highly purified CBD.[67] Outside of CYP-related drug interactions, clinicians should be careful of additive adverse effects when CBD is used concomitantly with certain medications, such as CNS and respiratory depression with depressant medications (e.g., benzodiazepines, barbiturates, morphine, and insomnia agents).[4] Thus, clinicians should carefully ask about prescribed medications, over-the-counter medications, nutritional supplements, and unapproved medication use, such as CBD, to avoid drug-drug interactions.

Monitoring is also a key element to promote patient safety with CBD use. Transaminase (aspartate aminotransferase, alanine aminotransferase) and bilirubin levels should be checked at baseline then at 1, 3, and 6 months after initiation and periodically thereafter to ensure early identification of any liver damage. Other monitoring parameters could include vital signs such as heart rate and blood pressure. Jadoon et al[68] conducted a randomized, double-blind, placebo-controlled, crossover study with the aim to assess CBD's impact on cardiovascular response. They found that with acute administration of 600 mg of CBD, patients had lower blood pressure (−5 mm Hg; $p < 0.05$), reduced stroke volume (−13 mL; $p < 0.01$), and an increased heart rate (+10 bpm; $p < 0.01$).[68] While this was a small single-dose study, the evidence suggests the need to monitor patients' blood pressure and heart rate at each visit throughout therapy with CBD, especially in patients with comorbid cardiovascular conditions and when increasing doses.

Further, the most common vehicle for CBD products are edible oils such as olive oil, grapeseed oil, and sesame oil.[4,69] Epidiolex, for example, is made with sesame seed oil. [4] With the increasing prevalence among children of severe allergies to foods, including peanut and sesame products,[70,71] clinicians must guide parents to select products with third-party testing to verify the inactive ingredients in these cases or recommend against use altogether.[72] Furthermore, administration of CBD in lipid formulations has been shown to increase absorption of CBD by as much as 300% compared with non–fat-containing formulations.[73] Thus, it is important for providers to carefully counsel caregivers on the risks of allergic reactions and excessive exposure when using oil formulations of CBD products.

Little is known about the safety of CBD in pregnancy, including effects on embryonic development, the risk of major congenital malformations, pregnancy outcomes, and postnatal outcomes including long-term neurocognitive effects. Preliminary data from rodent models suggest that CBD exposure *in utero* is associated with decreased problem-solving behaviors in exposed offspring.[74] Thus, the use of CBD during pregnancy should be avoided. The use of CBD during breastfeeding has also not been studied. However, owing to detection of CBD in breastmilk in women using marijuana, and the risk of product contamination with THC and other substances, discontinuation of CBD or avoidance of breastfeeding is recommended.[75,76]

Recommendations on Pediatric CBD Use for Clinicians and Public Health Organizations

With nearly one-third of parents (31.3%) reporting pediatric administration of an unapproved CBD product for ADHD, ASD, and/or GAD,[43] clinicians should specifically ask parents and patients about the use of CBD products, particularly in children with behavioral health diagnoses and neurodevelopmental disorders. Often parents may not think of CBD products when asked questions about medications during the medication reconciliation process. Parents may also not consider CBD as a dietary supplement. Thus, asking specific, nonjudgmental questions about CBD use can be helpful in soliciting this information from parents. In the authors' experience, asking open-ended questions about other products or services parents use to "enhance the health" of a child often opens dialog related to complementary and alternative treatments, including CBD.

When addressing unapproved CBD product use in children, the ARMED approach may provide a useful rubric for clinicians.[77] Originally developed as a tool for discussing complementary and alternative therapies with parents, this approach focuses on A-asking effective questions, R-respect family's perspectives, D-demonstrating respect for parents, M-monitoring therapy, E-providing proper education, and D-distributing information in a nonjudgmental, evidenced-based manner.[77] For example, if a parent comes to the pharmacy asking for CBD gummies to help her child with ADHD, using the ARMED approach may help the pharmacist ask questions about other therapies used for ADHD and listen respectfully to discern the parent's rationale and perceptions of CBD use. The pharmacist could also ensure that there is a connection to primary care for monitoring of therapy and could provide information on the efficacy and safety of CBD products, using evidence without passing judgment on choices.

Multiple studies indicate the importance of the clinician having a conversation surrounding CBD use with a nonjudgmental approach.[78] Other approaches that could be used when discussing CBD products include motivational interviewing, which is a patient-centered approach that follows similar principles to the ARMED approach. This could be a particularly beneficial approach when parental knowledge and health beliefs need to be explored in an encounter. Parents often perceive that clinicians lack significant knowledge regarding CBD products, so it is important for those working with pediatric patients to enhance their knowledge of potential uses, along with safety and efficacy data, surrounding CBD products.[78,79] Key educational messages for clinicians to share with parents are included in Figure 2. Public health officials should partner with local poison centers and local clinicians to understand regional usage patterns and concerns, as this may uncover opportunities for monitoring and education of the public. These parties should also be familiar with federal and state legislation and regulations regarding the use of CBD products. Clinicians, public health officials, and parents should be involved in reporting adverse reactions associated with CBD-containing products through the FDA's MedWatch reporting system. Local health departments, regulatory agencies, and clinicians should work together to disseminate up-to-date information on the risks and therapeutic potential of CBD. Lastly, resources aimed at providing evidence-based information on unapproved CBD products should be created and distributed to both parents and adolescents. Social media communication strategies may be helpful for public-facing communication.

Recommendations for Future CBD Research

To truly elucidate the role that CBD plays in the treatment of pediatric conditions, additional research is imperative. The true extent of unapproved CBD product use in the pediatric population is still unknown and warrants further study. Exploring the relationship between parent perceptions, knowledge, and health behaviors could help the medical community identify key areas for intervention. Research to establish evidence-based approaches to educating clinicians, parents, and children on the risks of unapproved CBD use should be prioritized.

In clinical research studies involving CBD, reliable, purified, pharmaceutical-grade CBD products should be used. While CBD products show promise for several conditions in children as previously discussed, placebo-controlled trials should be supported to establish efficacy and safety. Based on the current literature, GAD and neurodevelopmental conditions, including ASD and ADHD, should be a primary focus of this research. Trials evaluating the use of CBD products in children with various forms of epilepsy, ASD, behavioral concerns in patients with intellectual disability (NCT04821856), anxiety (NCT05324449), youth alcohol disorder (NCT05317546), and youth at risk for psychosis[80] are ongoing and may help to answer some of these questions. Additionally, long-term efficacy and safety must be established, including evaluation of the effects of CBD on the developing brain. Future research should also focus on pharmacogenomic factors that affect CBD pharmacokinetics and pharmacodynamics across the lifespan.

Conclusion

CBD is an effective antiseizure medication in pediatric patients diagnosed with Lennox-Gastaut syndrome, Dravet syndrome, or tuberous sclerosis complex. While data evaluating the use of CBD for indications other than seizure treatment continue to grow, the application of these data to clinical care is limited owing to variability in product composition, differing routes of administration, variance in dosing strategies, concerns for product integrity, and small sample sizes. The use of unapproved CBD products among children and adolescents continues to increase despite a lack of clinical data supporting use. These products seem to be used more commonly to treat behavioral concerns in pediatric patients, including ADHD, ASD, GAD, and sleep disorders in the pediatric population. Clinicians,

Figure 2. Key educational messages for parents about unapproved CBD products

- Only one CBD product (Epidiolex®) has been approved by the FDA and is used to treat seizures in children with certain types of epilepsy.
- CBD products sold in stores are not checked by the FDA and only 1 out of every 4 products contains the dose listed on the label.
- Store-bought CBD products may contain THC (the part of marijuana that makes you "high"), pesticides, or other substances that can hurt your child.
- To date, there is little scientific proof that CBD helps with conditions other than epilepsy in children.
- The safe and effective dose of CBD for children is unknown when using store-bought products.
- Common side effects of CBD include being sleepy, not wanting to eat, diarrhea, and changes in growth.
- CBD can damage the liver, especially when taken with seizure medicines.
- CBD can change how other medicines work in your child's body, which can cause serious problems.
- Always tell your child's providers and pharmacist about any CBD products your child is taking.
- CBD products made with oils like sesame, soybean, or sunflower oil can cause serious allergic reactions in children with food allergies.
- Using CBD during pregnancy may harm the baby's development, and CBD passes into breast milk during breastfeeding.
- CBD laws are different in each state and may not be fully legal.

public health officials, and health care leaders must be prepared to address the ramifications of increasing use of unapproved products in the pediatric population through ongoing evaluation of usage patterns, provision of evidence-based education, reporting of adverse effects to the FDA, and support of further research in the field.

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