

# LABORATORY SIMULATION TO IMPART SAFE USE OF CBD-RICH EXERTS

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*Abstract-Laboratory simulation as a method to teach evaluation of efficacy and safety of botanical oils for skin care applications can stimulate students to develop scientific reasoning and increase their knowledge by providing additional resources and materials that relate to differential bioactivity and potential overuse toxicity associated with their topical application to the skin. As a nonintoxicating, pharmacologically relevant constituent of hemp oil, cannabidiol (CBD) exerts a number of skin health promoting effects, including anti-inflammatory and neuroprotective activity. While CBD-rich hemp is widely touted as a miracle panacea to manage skin ailments, hemp tissues used to produce hemp may become contaminated by THC-rich trichomes of hemp flowers and thus acquire THC. In this study, we investigated the use of role play and scenarios to educate students about the therapeutic potential of CBD-rich hemp and promote active learning, critical understanding, teamwork, and leadership towards addressing the putative side effects associated with its use. The scenarios reproduced skin care situations in the beauty salon industry which allowed us to evaluate and discuss exposure to Cannabis-derived CBD and THC. Four additional fact sheets focused on dermatological, toxicological, neurological and psychiatric aspects of Cannabis use assisted with reflections and debriefing of the students. The strategy presented here can facilitate the teaching-learning process of students, and can be easily transferred and applied in other educational institutions for the safe and effective method to study application of botanical to skin care.*

**Keywords:** Skin care, dermatological, toxicological, neurological, CBD exerts

## Introduction

The use of a laboratory simulation as a teaching technique is widely encouraged due to its ability to promote active learning, critical understanding of the topic at hand, reasoning, decision making, teamwork and leadership. Considering the recent recognition of CBD-rich hemp in the general population, consumer industry, and medical environment, laboratory simulation can be an effective form of teaching in undergraduate scientific and medicinal courses. CBD-rich hemp is a complex botanical mixture originating from *Cannabis sativa* L. Studies have shown that students are unable to distinguish the derivatives of Cannabis (Atakan, 2012). Furthermore, students often associated four derivatives of Cannabis interchangeably: hemp, medical CBD, medical THC and marijuana. As a result, difficulties have arisen when understanding the usage and benefits of hemp vs. medical CBD vs. medical THC vs. marijuana. Not everyone who used the derivatives of cannabis were affected in the same way – a

common misconception common among consumers (Atakan, 2012). There is a need for the creation of courses and/or stimulations focused on improving students understanding of this subject. Marijuana term refers to Cannabis flower and leaf tissues that contain high amounts (~20%) of THC and low amounts (~2%) of CBD. Marijuana can be used both recreationally and medicinally.

There are many negative insinuations associated with THC, many of which lead to psychological and psychotic disorders. On the other hand, hemp, also commonly referred to as industrial hemp, is a selected group Cannabis cultivar that contain high amounts (~15%) of CBD and less than 0.3% of THC (Brutlag&Hommerding, 2018). Uses of industrial hemp include: hemp, food, and clothing. Industrial hemp can be refined to create CBD-rich hemp. Understanding how CBD-rich hemp plants are agriculturally bred is a good way to differentiate CBD from THC and how it might affect the body.

CBD-rich hemp can be extracted in three different ways: CO<sub>2</sub> method, method, and ethanol method. Given this relationship, laboratory simulation as a method to teach can stimulate students to understand and differentiate the various derivatives of *Cannabis sativa L.*, to develop clinical application and increase the confidence of their knowledge on CBD-rich hemp specifically.

The preparation of scenarios and role play is a crucial component for success of the simulation, and discussion of each role play among groups is important for educational purposes (Almeida et al., 2015). Based on the need to incorporate new methods in the teaching and learning environment on this subject, a case study laboratory simulation has been developed for undergraduate students in scientific and medicinal courses.

### **Methods**

This study reports the experience of creating and utilizing a case study for laboratory simulation for undergraduate students; the simulation was developed as part of the activities of the undergraduate and graduate Food Chemistry and Bioprocessed Materials course at the North Carolina State University in 2018. The objective of the case study was to provide a template for undergraduate students in scientific or medicinal courses to develop scientific application and decision-making when assessing CBD-rich hemp. Those responsible for assessing the simulation were an MS student in a class setting with eight peer graduate students, and a professor with expertise in food science.

The scenario was applied to undergraduate students who were in their third and fourth years in either food science, nutrition, or bioprocessing. This activity can be further explored in other scientific and medicinal courses. For transfer and application of this simulation to other educational institutions, the facilitator of the activity will be responsible for providing key information during the scenario to guide students in scientific reasoning and subsequently, overseeing a questionnaire. The participants of the case study will be divided into groups and assigned a health professional involved in the study:

dermatologist, toxicologist, neurologist or psychiatrist. One person in each group will then take on the role of the health professional. This allows students to actively participate, make choices, receive feedback, and refine their understanding of the concept while adding dramatization to make the experience seem more real (Cogo et al., 2017).

Subsequently, students will be given an additional role and asked to determine the efficacy of using CBD-rich hemp in the following health-related outcomes: psoriasis, epilepsy, psychosis, and pregnancy. Among the expected results from the laboratory simulation, we focused on active learning, reasoning among groups, post-simulation discussion and decision-making on the use of CBD- rich hemp.

### **Results**

In the scenario of using of CBD-rich hemp oil in a tanning bed, the objective was to evaluate what happened to the individual. The student/group(s) had to investigate the symptoms the individual experienced, identify the factor that caused the symptoms and discuss the results. Students used the fact sheets provided to identify the relationship among the symptoms and CBD-rich hemp, if any.

Subsequently, students were asked to evaluate an additional factor and determine the therapeutic potential of using CBD-rich hemp in each instance. During the debriefing the participants had the opportunity to reflect on their potential actions, skills, decision-making and the possible treatments that should be used in that case.

### **Case Study Analysis and Role Play**

The case study was organized in the form of four discussion groups that focused on different dermatological, neurological, psychiatric and toxicological aspects of using CBD-rich hemp oil for skin health applications. Subsequently, each group was assigned an additional factor that should be taken into consideration. The additional factor correlated with the family members field of study. The study will follow the outline as described in Chart 4.1.

TABLE 3.1.OUTLINE FOR GROUP DISCUSSION AND ROLE PLAY.

Time	Action expected from participants	Role Play
0-9 min	Break into four groups.	Each group will take on the role of one of the family members. Each group will be given a fact sheet summarizing the positive and negative effects of CBD rich hemp in relation to their field of study. Choose a group leader.
10-19 min	Read over fact sheets.	Discuss fact sheet, health conditions and answer the questions. Do not share any information with the other groups (i.e. family members).
20-24 min	Read over additional factor that correlates with the family members field of study.	Discuss additional factor among your group.
25-34 min	Discussion.	Discuss whether subject should use CBD rich hemp going forward and whether CBD rich hemp is appropriate to use with the 'additional factors.' Try to convince the entire group that your viewpoint on CBD rich hemp is the most reasonable. Come to an agreement with justification.
35-50 min	Reconvene as a class.	Group leader will present your groups viewpoint on subject situation and the additional factor.

**Background information on four additional factors**

**Group Two: Epilepsy**

Your one-year-old cousin suffers from a rare epileptic seizure known as Dravet syndrome (DS). The medications used for treatment are often times ineffective when controlling the episodes. Dravet syndrome is a genetic condition that appears early in life involving frequent, fever-related seizures (Gaston & Szaflarski., 2018). CBD (Epidiolex) was recently approved by the FDA for controlling DS episodes; however, there are age restrictions for use of CBD-rich hemp on individuals with DS. Is using CBD-rich hemp oil an effective form of treatment?

**Group Three: Psychosis**

CBD-rich hemp can reduce psychotic, anxiety and withdrawal symptoms through the modification of neurotransmitter signaling and functional cerebral changes (Mandolini et al., 2018).

**Group Four: Pregnancy**

You are a three-week pregnant female with no history of any health conditions. You have been told that marijuana use during pregnancy can cause impaired fetal development of neurons. In rare instances, some commercially marketed hemp could lead to mild cannabinoid poisoning in children and

pregnant women (Yang et al., 2017). If using CBD-rich hemp while pregnant, will there be similar adverse effects?

**Role-Play Fact Sheet for Tracy (Dermatologist)**

In the human body, skin is one of the largest organs. Skin has two distinct layers – the epidermis and dermis. The epidermis consists of tightly packed keratinocyte layers and serves as a protective barrier against bacterial contact and environmental interactions. Resident immune cells also help to maintain this protective barrier (Eagleston et al., 2018). The dermis is composed of collagen, adaptable fibers, and an assortment of extracellular matrix proteins (Chelliah et al., 2018). Dermal layer also contains blood and lymphatic vessels, nerve endings, fibroblasts and a mixture of immune cells (Hashim et al., 2017). Overstimulation of immune cells in the skin can promote excess cellular permeation and apoptosis, resulting in inflamed skin and autoimmune disorders. Autoimmune disorders of the skin often lead to secondary complications such as open wounds/cracks in the skin and bacterial infections. Until recently, steroids have been the most effective form of treatment, but their long term use ultimately damages the skin. The prevalence of topical cannabinoids, specifically CBD rich hemp, has risen sharply in clinical dermatology. CBD rich hemp offers a safe and natural means

to manage atopic dermatitis (AD), psoriasis, acne vulgaris and skin cancer (Hashim et al., 2017). Atopic dermatitis, commonly referred to as eczema, is the itchy inflammation of the skin. The main symptom is a rash that appears on the arms and behind the knees. Recent studies have suggested that atopic dermatitis can be managed by cannabinoids and topical agonists of cannabinoid receptors (Hashim et al., 2017). Psoriasis is an inflammatory disease characterized by raised scaly skin, erythema, and hyperkeratosis (Chelliah et al., 2018). The course of disease is often unclear. CB2 receptor agonist reduced recruitment of mast cells and a decreased blood concentration of histamine suggesting that CBD can be a useful topical agent for skin conditions related to mast cell activation (Hashim et al., 2017). Acne vulgaris is a condition that occurs when skin cells plug hair follicles. The hair follicles are blocked by and dead cells (Eagleston et al., 2018). A single randomized clinical study reported the effects of 3% cannabidiol infused cream on acne vulgaris (Ali et al., 2015).

When applied twice a day for 8 weeks to infected areas, the CBD cream significantly decreased the acne present in comparison to a control group. Abnormal growth of skin cells can lead to skin cancer. There are three common types: squamous cell carcinoma, basal cell carcinoma, and melanoma. Squamous cell carcinoma is caused by the uncontrollable growth of aberrant squamous cells (Parekh & Seykora, 2017). Basal cell carcinoma begins in the basal cells. Basal cells function to produce new skin cells and lie underneath squamous cells (Pellegrini et al., 2017). Melanoma is the most aggressive and serious type of skin cancer (Ko, 2017). Melanoma, basal, and squamous cell carcinoma express cannabinoid receptors, CB1 and CB2. CB2 plays a greater role in inducing apoptosis of cancer cells than CB1. CB2 decreases the expression of endothelial growth factor, inhibits melanoma progression, and reduces cancerous cells ability to metastasize (Eagleston et al., 2018).

**Table 3.2. Debriefing – Dermatologist fact sheet.**

<b>Questions to discuss among Tracy’s group</b>	
1	Is it possible to experience adverse symptoms if using CBD-rich hemp for the first time on your skin?
2	Is CBD-rich hemp anti-microbial?
3	Which type of skin cancer, squamous, basal or melanoma is CBD-rich hemp most effective in treating?

**Role-Play Fact Sheet for Ivy (Toxicologist)**

Over the past decade, the legality of marijuana, both recreationally and medically has changed dramatically across North America, specifically in the United States and Canada. Some states allow for the recreational use of cannabis whereas others strictly limit cannabis for medicinal purposes (Brutlag&Hommerding, 2018). Recently, Canada passed a law to allow both recreational/medicinal use of cannabis. The legality of transporting cannabis across state borders for medicinal and research purposes has recently changed in the United States.

There are four different forms of cannabis: marijuana, hemp, medical CBD and medical THC. Of the four, medical CBD is

the only one that has no psychoactive properties. The THC concentration present in marijuana is 15% whereas the concentration of CBD is less than 0.3% (Brutlag&Hommerding, 2018). If asked to take a drug test while using CBD, whether orally or topically, there would be no trace amounts of THC present in the urine. In relation to its constituents and physiological properties, cannabinoids are complex plants that can have opposing effects. Cannabinoids chemical profile and pharmacology have yet to be fully understood. Containing oxygen and aromatic hydrocarbon compounds, cannabinoids compose 70 of the 400 constituents in Cannabis sativa L (Inci et al., 2017). Three recent reviews assessed the safety and efficacy of CBD. One study concluded

that CBD-rich hemp does not alter food intake, affect heart rate, blood pressure, and body temperature even with repeated use at doses as high as 1,500 mg a day (Iffland&Grotenhermen, 2017). However, in vitro and animal studies on the effects of CBD hemp extract suggest that at high doses of cannabinoids, adverse toxicological effects occurred (Marx et al., 2018). Another observation is the that “plant-based” and “purified” CBD-rich hemp oil can be used at different doses. Individuals using a plant-based extracts of CBD reported using a significantly lower dose in comparison to purified CBD (Pamplona, da Silva, Coan., 2018). When

using CBD-rich hemp, adverse effects can occur. Individuals report experiencing adverse effects when using purified CBD-rich hemp oil instead of plant-based extracts. The most common reported adverse effects include: appetite changes, sleepiness, gastrointestinal discomforts, diarrhea, weight changes, fatigue, and nausea (Pamplona, da Silva, Coan., 2018). When paired with other drugs, further adverse effects occurred, specifically when used on individuals with epilepsy. Direct CBD toxicity should not be associated with adverse effects, but drug interaction. Further studies are needed to assess the toxicological effects of CBD extract.

**Table 3.3. Debriefing – Toxicologist fact sheet.**

<b>Questions to discuss among Ivy’s group</b>	
1	At what dose are cannabinoids considered toxic? Does this apply to both animals and humans?
2	What percentage of CBD is found within CBD-rich hemp oil?

**Role-Play Fact Sheet for Jack (Neurologist)**

CBD produces neurological effects in the body by modulating CB1 cannabinoid receptors. CB1 cannabinoid receptors are located in the motor system, cortex, limbic system, amygdala and hippocampus. CB1 receptors augment the release of presynaptic dopamine (Bonaccorso et al., 2018). Recent studies suggest CBD hemp oil as an effective solution for treating multiple neurological diseases such as epilepsy, Alzheimer’s disease and Parkinson’s disease. Epilepsy is a neurological disorder characterized by episodes of sensory disturbance, episodes of unconsciousness, unusual electrical activity in the brain, resulting in epileptic seizures (Gaston &Szaflarski, 2018). Although there is no cure for epilepsy, medications,surgery, devices, or dietary changes can offer some relief. In two specific epileptic conditions, Lennox-Gastaut syndrome (LGS) and Dravet syndrome (DS), medications are often times ineffective (McCoy, 2018). After reviewing the safety and efficacy of CBD-rich hemp oil for treating epilepsy, the FDA approved the use of CBD (GW Pharmaceutical’s Epidiolex) for both Lennox-Gastaut syndrome and Dravet syndrome (McCoy et al., 2018). Use of Epidiolex for individuals with epilepsy helps to alleviate pain

associated with seizures and can reduce further neurodegenerative conditions associated with epilepsy (Pamplona, da Silva, Coan., 2018). Alzheimer’s Disease (AD) is a neurodegenerative disease. The accumulation of beta-amyloid plaques and tau tangles destroy neuron connections within the brain (Watt & Karl, 2017). Damages in cortex and hippocampus results in impaired memories. Currently, there are no forms of treatment that stop or reverse impairments caused by AD. However, CBD has been investigated as a potential treatment option for AD. Research suggests that CBD was able to prevent the development of social recognition deficit in individuals with Alzheimer’s disease. CBD could help individuals with Alzheimer’s to recognize familiar faces (Watt & Karl, 2017). This is the first evidence that suggests CBDs ability to slow the detrimental progression of Alzheimer’s disease. Parkinson’s disease is a central nervous system (CNS) disorder that affects movement. Symptoms are gradual, starting with a slight tremor in one hand (Crippa, 2018). Although tremors are a common symptom, stiffness or slow movement can also occur (Ganos, 2018). CBD may help to improve motor impairment in individuals with Parkinson’s disease. CBD can also target

psychotic symptoms of individuals with Parkinson’s disease (Crippa, 2018). CBD modulates cell fate regulatory pathways such as autophagy for neuronal survival in neurodegenerative

experimental models, suggesting the potential benefit of CBD treatment for psychiatric/cognitive symptoms associated with neurodegeneration.

**Table 3.4. Debriefing – Neurologist fact sheet.**

<b>Questions to discuss among Jack’s group</b>	
1	At what age is it safe to use Epidiolex on children with Dravet syndrome? Is the dosage body weight dependent?
2	How does CBD-rich hemp oil help individuals with epilepsy?
3	During what stage of Alzheimer’s Disease can CBD-rich hemp oil help individuals recognize faces?
4	What psychotic symptoms can CBD-rich hemp oil target in individuals with Parkinson’s disease?

**Role-Play Fact Sheet (Psychiatrist)**

Fear and anxiety are adaptive responses essential to managing threats to survival. The autonomic nervous system works to adapt and respond to your immediate environment. During high emotions, the sympathetic nervous system produces a ‘fight or flight’ response (Richards, 2017). During feelings of relaxation, the parasympathetic nervous system is activated, lowering your heart rate and blood pressure (Richards, 2017). This necessary and adaptive system is responsible for feelings of anxiety. Marijuana and THC infused products have been known to trigger or amplify feelings of anxiousness and paranoia. However, CBD rich hemp oil is gaining major traction in the medical world, as people praise its ability to reduce anxiety in people with certain related disorders. Generalized Anxiety Disorder (GAD) is defined as the persistent and excessive worry that interferes with daily activities. Areas in the brain involved with emotional processing and heightened amygdala response activation are often associated with anxiety disorders, such as general anxiety disorder (Noel, 2018). Acting as an agonist to 5-HT1A receptor and GABAA receptor, CBD rich hemp oil decreases heart rate and blood pressure, ultimately reducing the anxiety-related behavior associated with GAD (Resstel et al., 2009). Stress and experiencing a traumatic event lead to the development of post-traumatic stress disorder (PTSD).

Individuals diagnosed with PTSD may feel anxious or scared even when they are not in danger (Blessing et al., 2015). The systemic administration of CBD rich hemp oil reduces the acute increase in heart rate and blood pressure induced by stress. These anxiolytic effects depend upon CB1 receptor activation (Bonaccorso et al., 2018). CB1 receptors in the brain deal with movement, pain, emotions, mood, thought process, and memories. Social anxiety disorder is an intense fear of being judged, evaluated negatively, or rejected in a social environment. When validating the effects of CBD on social anxiety disorder, using a Simulated Public Speaking Test (SPST) predominates because the fear of public speaking is a prime example of the illness. It is suggested that CBD’s anxiolytic action may be mediated by the 5-HT1A receptors (Noel, 2018).

**Table 3.5. Debriefing – Psychiatrist fact sheet.**

<b>Questions to discuss among group</b>	
1	At what dose of cannabidiol is needed to produce the desired anxiolytic effect? Would this dose differ among various anxiety-related conditions?
2	How long would CBD rich hemp oil have to be administered before there is a decrease in anxiety-related conditions?
3	If paired with other medications, will CBD rich hemp oil cause an adverse effect?

**Discussion**

Laboratory simulation is an effective form of teaching. Using this method allows students to engage in critical thinking, work as a team and develop leadership skills. The construction and use of a laboratory simulation are valuable approaches that must be based on scientific reasoning, clinical evidence, reviewed by peer graduate students and undergo a series of trial runs. Thus, the construction and formatting of a case study used in laboratory simulation must be paired with feedback from students, peers, facilitators and professors. A carefully formatted case study and stimulation combination enhances learning through processing, adaptation, and discussion (Almeida et al., 2015). In practice, students are able to enhance their understanding of CBD-rich hemp oil and its application to human health. The facilitators must be familiar with the topics discussed in the case study before contributing to the laboratory simulation. During the simulation, the facilitators must be available to answer questions and help guide the students towards the desired goal. Therefore, formatting the case study to reach the intended goal is imperative, including adding dramatization to the dialogues to make the experience seem more real and clearly defining the objectives. The use of role play, fact sheets and additional factors for each group to take into consideration comprised the success of the case study and simulation. Subsequently, discussing each groups viewpoint as a class allows for collaboration, debate and in some cases, concession. The laboratory simulation and case study demonstrate the various therapeutic potentials of CBD-rich hemp oil. Although CBD-rich hemp oil is a newly discovered phenomenon and remains a Schedule I controlled substance, treatments using CBD-rich hemp oil are effective and safe in relation to atopic dermatitis,

psoriasis, acne vulgaris, skin cancer, epilepsy, Alzheimer’s disease, Parkinson’s disease, generalized anxiety disorder, post-traumatic stress disorder, and social anxiety disorder. CBD-rich hemp oil can act as an anti-inflammatory and anti-bacterial agent, two crucial events that can prevent mast cell activation in individuals with psoriasis and atopic dermatitis (Hashim et al., 2017). Also corresponding to inflammation, acne vulgaris can be treated with CBD-rich hemp oil; the production of sweat by the sebaceous glands is lowered, leading to a reduced accumulation of acne (Ali et al., 2015). The spread of skin cancer can be prevented by use of topical CBD-rich hemp oil; cancer cells undergo induced apoptosis and are unable to metastasize (Eagleston et al., 2018). In epileptic conditions, CBD-rich hemp oil can put individuals at ease during seizures and help to lower neurodegeneration associated with epilepsy (Pamplona, da Silva, Coan., 2018). The majority of the individuals used in each study obtained substantial benefits from the use of CBD-rich hemp oil and if adverse effects were to occur, they were mild and minimal.

**Conclusion**

The construction of scientific simulation scenarios focused on the evaluation of botanical oils and their application to skin health allowed the students, as well as the teachers, to develop scientific reasoning more accurately, thus, promoting safer skin care. The participants could live situations close to real ones in a controlled laboratory environment, thus, being able to perform tasks and procedures without causing harm to consumers. Given the growing number of consumers with interest in hemp-and marijuana-based products, and the availability of new botanical extracts for management of skin ailments, there is a critical need for courses and teaching strategies that effectively promote learning, assist in the

preparation of students and professionals, and ensure the cost-effectiveness when choosing the treatment.

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