**Assignment 4.1**

**Considerations for** **formulating a cannabinoid-containing drug product for inhalation**.

There are many considerations to making a cannabinoid product for inhalation. The biology of the lungs, the delivery method, the extraction method and additives, all play a roll in of a product is developed. All three factors have to be in sync to produced a product that has high cannabinoid bioavailability.

When formulating a cannabinoid – containing product for inhalation it is important to consider how the body functions and how this process can be utilized to deliver cannabinoids with high bioavailability.

The lungs are the place in the body where the exchange of oxygen and carbon dioxide in and out of the blood stream. Air travels through the mouth down the esophagus to the lungs. Once inside the lungs air is moved around from the force of the diaphragm muscle located under the lung’s lower lobes. Air is pushed through the network of bronchial tubes in the lungs commonly referred to as the Bronchial “Tree” due to is similar resemblance when inverted. At the end of the bronchial tubes are alveoli which allow oxygen to move in and out of the blood stream along with Carbon dioxide. This also where the inhaled cannabinoid formula will enter the blood stream. The importance of this of this is that inhalation of cannabinoids bypasses the “1st Pass” metabolism in the liver. This means that inhalation will have a faster route to the body’s blood stream than through the stomach.

There are many ways to inhale cannabinoids. They can me smoked, vaporized, used in a MDI (Metered Dose Inhaler) or Nebulizer. And each way has advantages and disadvantages. Smoking and Vaporizing dosage depends on the user to regulate amounts inhaled. While MDI devices, such as inhalers or nebulizers can consistently give equal amounts with out user control. This makes MDI the preferred choice for pharmaceutical companies as they want consistent controlled dosages.

Based on which device we choose will determine how formulate the product. If we know we want a dry powder inhaler, then we would go about the formulation process different than we would if we were looking for a substance that could be “vaped”.

We first start with Decarboxylation. Decarboxylation is the removal of a carboxyl group from the originating compounds CBDA and THCA which are found in cannabis flower **[1]**. Both CBDA and THCA are acids and must be converted to CBD and THC through decarboxylation. Only then will CBD and THC be able to get you “high”. This can be done by heat, light or mixing with solvents. When smoked cannabis instantly converts to CBD and THC. But when formulating a solution for a device the process of extraction and formulation become much more lengthy.

Our most common routes for extraction are oil based extraction, typical used to create edibles by placing raw cannabis flower in a oil solution since THC is lipophilic. Alcohol based extraction, which uses a substance such as Butane or Ethanol and comes with safety concerns as it is not pure. And CO2 based extraction, which is most preferred, as it leaves no toxic impurities but is highly complicated and costly.

The CO2 extraction process, the CO2 gas is both increased in pressure and temperature until it becomes “supercritical” state in which the CO2 acts as a liquid and a gas at the same time. This unique state allows it go pass through raw flower extracting the active compound and accumulating into a peanut buttery substance that is full of cannabinoids. Winterization (or freezing the alcohol extract) increases the purity of the THC/CBD substance increasing the potency to as high a 65%. And even after winterization, the substance can be distilled to increase its potency to the range of 75 – 90%

Once we have a potent substance, we can add emulsifying agents to prepare the substance for the devices when intend to use. At this time any compounds such a terpenes they may have been removed during extraction can be added back in the solution. Typical emulsifying agents are propylene glycol, vegetable glycerin. The important thing to consider here, is that some of the emulsifying agents have been tested for ingestion and topical application by humans. But some have not been tested for inhalation.

Ultimately this whole industry is so new that there is still room to discover new ways of creating substances and new ways to deliver them. If the product we were asked to make would be used in a clinical setting, or by prescription. The MDI would be the preferred choice. However if the product is to used for “recreational” purposes then vaping would be the most fitting. Like Dr. Minchom mentioned in his video lecture, it does not matter what best if the patient does not like the delivery system **[2]**.

References:

1. A beginner Guide to Decarboxylization – April 4th, 2021 – *Emily Kyle, MS, RDN, HCP*

[A Beginners Guide to Cannabis DecarboxylationCannabis decarboxylation must occur before cooking, baking, or extracting oil from the dried flower buds of the cannabis plant in order to reap the benefits of activated CBD or THC.Emily Kyle Nutrition](https://emilykylenutrition.com/cannabis-decarboxylation/)

2.   [Development and Delivery of Pharmaceutical Products (CMC) - MaRS Best Practices](https://youtu.be/B_yk0UlyQwE) [Video]. YouTube. https://youtu.be/B\_yk0UlyQwE. Published September 30, 2011. Accessed March 5, 2020

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Great write up. You touched on all the salient points!

