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Professional Portfolio

School

University of Maryland
School of Pharmacy

Program

Medical Cannabis
Science &
Therapeutics

Degree

Master of Science

THC and CBD Water Solubility

Objective: Apply concepts of pharmacology, pharmacognosy, pharmaceuticals, and pharmacokinetics to determine appropriate cannabis dosing, dosage forms and routes of administration for optimal treatment.

Context: Describe the diversity of compounds that are components of cannabis.

Description and Rationale: This piece of work describes how two prominent compounds in cannabis (THC and CBD) are lipophilic and what that means for oral administration method to achieve optimal therapeutic benefits. The paper provides considerations for pharmaceutical companies to consider when investing in cannabis therapeutics.

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Assignment 1.1: THC and CBD Water Solubility

With the human body being made up of mostly water, pharmaceutical companies look for drug advancements through chemical structures with high aqueous solubility.¹ When a drug is water soluble it is more easily distributed through the body by blood.¹ This process allows for traditional drugs to be administered orally to provide therapeutic benefits.¹ Hence, it is logical why pharmaceutical companies are constantly competing to bring new drugs to the market that are water soluble.¹

The chemical structure of medical cannabis compounds, such as delta-9-tetrahydrocannabinol (THC) and cannabidiol (CBD) make it difficult to develop a drug with these cannabinoids that meets the water solubility requirements of most pharmaceutical companies.¹ THC and CBD are fat loving (lipophilic) molecules that have poor water solubility.¹ This is because of their chemical structure. Both CBD and THC are composed largely of hydrocarbon rings and hydrocarbon tails.¹¹ Hydrocarbons are incredibly lipophilic, or fat soluble.¹ This is because the charge on these groups of atoms are evenly distributed, making them non-polar.¹ The longer the hydrocarbon tail the more fat loving the molecule.¹ Both CBD and THC have long hydrocarbon tails.¹ Because of this they do not mix well with water which consequently it makes it more difficult for them to be distributed throughout the body.¹

There are 545 compounds in medical cannabis to consider for therapeutic benefits.³ One group of compounds are called terpenes.¹ The terpene Myrcene, for instance, has a chemical structure of only hydrogens and carbons, making it extremely lipophilic.¹ When looking at cannabinoid and noncannabinoid constituents of medical cannabis, hydrogen and carbons are frequently dominating within the various chemical structures.³

THC and CBD are not 100% lipophilic.¹ They both have hydroxyls which allow the compounds to have some water solubility.¹ Hydroxyls are groups of Oxygen and Hydrogen, with a largely negative charge.¹ These negatively charged groups of atoms effectively polarize a molecule.¹ However, the ratio of hydroxyls to hydrogens and carbons is not enough to overcome the fat-loving dominating part of the chemical structure.¹ Cannabis for medicinal considerations has an uphill battle regarding traditional oral administration as a result of the fat loving, lipophilic chemical structures of its constituents.^{1,3} The chemical structure of the hydrocarbon trail and limited hydroxyls in both cannabinoids make it more difficult for THC or CBD to effectively get distributed through the body.¹

Hydrophilic, or water-loving drugs that are present in most medicine cabinets are mostly composed of polar molecules.¹ This is what makes them dissolve easily in water.¹ Although hydrophilic substances are more easily transported through the body, they are not always available to the cell.¹ Inside the human body cells all have a lipid bilayer that surrounds the

internal part of each cell.¹ The molecule that makes up the lipid bilayer of the cell membrane has a hydrophilic (polar) head of phospholipid and a hydrophobic (non-polar) fatty acid tail.² This combination creates a semipermeable cell membrane. In order for a substance to permeate the cell membrane, it needs to pass through the polar head and the non-polar center of the lipid bilayer.² Thus substances should be lipophilic to some degree for easy passage through the cell membrane.¹ THC and CBD molecules' unique lipophilic structure with some hydrophilic hydroxyl components make them more readily permeable to the cell membrane.¹ This is a benefit that should also be considered by pharmaceutical companies when investing in these compounds as therapeutics.

References:

¹ Coop, A. Introduction to Chemistry of Compound in Cannabis. Module 1 Video Lectures and PowerPoints.

https://blackboard.umaryland.edu/webapps/blackboard/content/listContent.jsp?course_id=_18328_1&content_id=_1897223_1. Accessed March 20, 2020.

² The Editors of Encyclopaedia Britannica. Membrane. Encyclopædia Britannica.

<https://www.britannica.com/science/membrane-biology>. Published January 13, 2020. Accessed March 22, 2020.

³ Pertwee RG. Handbook of Cannabis. Vol First edition. Oxford: OUP Oxford; 2014.

<http://search.ebscohost.com.proxy-hs.researchport.umd.edu/login.aspx?direct=true&db=e025xna&AN=853248&site=ehost-live>. Accessed March 22, 2020.