Salvestrol Inhibitor in Review: CANNABIS

- Inhibits CYP1B1 EROD enzyme activity
- CBD binds irreversibly to CYP1B1
- Inhibits or potentiates action of other pharmaceuticals
- Greatly decreases therapeutic benefits of Salvestrol
- Successful use in end of life palliative care setting not in active care

There is a lot of interest surrounding the use of Cannabis in cancer care with a strong call for clinical trials. Currently in use there are whole plant extracts and synthetic forms of active metabolites delta 9-tetrahydrocannabinol (Δ^9-THC), cannabidiol (CBD) and cannabinol (CBN). They are mainly used in end of life palliative care settings and more recently to curb the side effects of chemotherapy induced nausea, vomiting, cachexia and neuropathic pain.[1] The clinical benefits of Salvestrol are greatly reduced with concurrent use of cannabis.[2]

It is well documented that CYP1B1 enzymes are intrinsically elevated in all types of cancer cells and virtually undetectable in healthy cells.[3] Salvestrol bypasses first pass metabolism and selectively binds to the CYP1B1 enzyme within cancer cells to form an active compound which may bring about cell cycle arrest and trigger apoptosis.[3] This is the primary mechanism of action for Salvestrol.[3]

Yamaori et al. (2010) studied the major phytocannabinoids and their potential inhibitory effect on human CYP1 enzymes to confirm competitive inhibition of CYP1B1 EROD activity in a dose dependent manner. Inhibition of CYP1 EROD enzyme activity is only temporary and subject to half-life parameters with the exception of CBD which binds irreversibly.[4]

Pre-clinical data suggests cannabinoids to have anti-tumour action, however all the research is based on animal studies and is yet to be replicated in human trials.[1,5]

The only study conducted in humans was administered intra-cranially to patients with glioblastoma multiforme.[1] The contra-indication of concurrent cannabinoid use in natural or synthetic form with Salvestrol is due to competitive inhibition of CYP1B1 enzymes.[2] CBD has been identified to have greater inhibitor effects of CYP enzymes than grapefruit.[4]

Cannabis administered orally has a variable bioavailability of 6-20% with peak plasma concentrations 1-6 hours after administration.[6,7] The terminal half-life is 20-30 hours. Inhaled administration has a bioavailability of 10-35% with peak plasma concentrations in 2-10 minutes that rapidly decline over 30 minutes.[6,7] Obviously bioavailability varies according to depth of inhalation, puff duration and breathhold.[7] Inhalation with the use of tobacco inhibits Salvestrol action by increasing carbon monoxide levels that irreversibly bind to CYP1B1 enzymes.[3] It is widely acknowledged that marijuana smoke contains procarcinogens that contribute to high rates of DNA damage and mucosal abnormalities along which are highly correlated to airway cancer.[8]

Further investigation to validate anti-tumor capabilities of cannabinoids is warranted, however it has well documented benefits for use in a palliative care setting to enhance end of life symptoms. Given the inhibition of cannabinoids on the CYP enzymes, it has the potential to inhibit or potentiate effects of other pharmaceutical substances which are beyond the scope of this review. In the case of Salvestrol, cannabinoids inhibit the CYP1B1 enzyme which is pinnacle to the mode of action. Concurrent use of cannabinoids greatly decreases the therapeutic value of Salvestrol therefore significantly reducing clinical benefits of supplementing.

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