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ANANDA DEVELOPMENTS PLC

Ananda's ambition is to be a leading UK grower and manufacturer of consistent, high-quality medical cannabis for UK patients.

Medical Cannabis Research Roundup

Issue Nineteen

Summary:

The last month has seen more evidence of cannabis and its constituents including the reviews of the pharmacological effects of cannabidiol, its potential in eye health, prostatitis and chronic pelvic pain and general chronic pain. To illustrate some of the wide effect cannabis and some of its constituents such as cannabidiol and terpenes we have chosen three papers on quite different subjects.

The first is on acne, something that everyone can relate to. What the study demonstrates is that cannabidiol (CBD) plus terpenes, in this case from a pennywort, a traditional herbal medicine plant, have a better effect than CBD by itself. This is not surprising given the anti-microbial properties of terpenes and the involvement of microbes in acne. Cannabis also contains terpenes, so it is likely that a broad or full spectrum cannabidiol topical might have similar effect.

Another example of the benefits of a broad or full spectrum of cannabinoids and terpenes is shown in the paper on the synergistic activity of THC and terpenes compared to THC alone in the second paper.

The third paper exemplifies the benefits of CBD cannabis to general health showing that people were better off in terms of less drowsiness lower diabetes higher testosterone.

Like many papers we have had in our Research Roundup before these show the many activities of cannabis and/or its constituents which is an example of the broad nature of the endocannabinoid system.

Good for acne

Acne vulgaris, the most common form of acne, is characterized by a mixed eruption of inflammatory and noninflammatory skin lesions primarily affecting the face, upper arms, and trunk.

The pathogenesis of acne is multifactorial and includes abnormal keratinization and plugging of the hair follicles, increased sebum production, proliferation and activation of *Cutibacterium acnes* (*C. acnes*; formerly *Propionibacterium acnes*, *P. acnes*), and finally inflammation.

The first stage of the study investigated the capacity of different plant extracts and plant extract combinations to reduce *C. acnes* growth and decrease IL-1 β and TNF α secretion from U937 cells. The results found that Centella asiatica triterpene (CAT) extract as well as silymarin (from *Silybum marianum* fruit extract) had significantly superior anti-inflammatory activity when combined with CBD compared to either ingredient alone.

In addition, the CAT extract helped potentiate CBD-induced *C. acnes* growth inhibition. The three ingredients were integrated into a topical formulation and evaluated in ex vivo human skin organ cultures. The formulation was found to be safe and effective, reducing both IL-6 and IL-8 hypersecretion without hampering epidermal viability.

Finally, a preliminary clinical study of this formulation conducted on 30 human subjects showed a statistically significant reduction in acne lesions (mainly inflammatory lesions) and porphyrin levels, thereby establishing a tight correlation between in vitro, ex vivo, and clinical results. Further studies must be conducted to verify the results, including placebo-controlled clinical assessment, to exclude any action of the formulation itself.

Reference:

Development of an Effective Acne Treatment Based on CBD and Herbal Extracts: Preliminary In Vitro, Ex Vivo, and Clinical Evaluation (hindawi.com) <<https://www.hindawi.com/journals/ecam/2023/4474255/>>

<<https://dim.mcusercontent.com/cs/fd0e56ff0828ad1078ee6b45e/images/87262912-5e96-101e-7cbf-8aade557dc8.jpeg?w=564&dpr=2>>



Evidence of synergistic effects of THC and terpenes

There has long been talk of the entourage effect of full spectrum cannabis and despite much discussion there has not been a lot of follow up work to provide more evidence of it - particularly in the entourage or synergy of cannabinoids and terpenes.

In this preprint of this study from Israel has provided in vitro evidence of the synergistic activity of THC and various terpenes at the CB1 receptor.

Importantly, the study showed this activity at the ratios of terpenes to THC that appear in the plant. The amount of total terpenes in cannabis flower tends to be approximately 2-3% w/w. Commonly, the three or four major terpenes will amount to about 50% of the total.

The results demonstrate that all terpenes, when tested individually, activate CB1 receptors, at about 10-50% of the activation by THC alone. The combination of some of these terpenes with THC significantly increases the activity of the CB1 receptor, compared to THC alone. In some cases, several fold.

For some terpenes, the activation obtained by THC- terpene mixtures is notably greater than the sum of the activations by the individual components, suggesting a synergistic effect. Our results strongly support a modulatory effect of some of the terpenes on the interaction between THC and the CB1 receptor.

As the most effective terpenes are not necessarily the most abundant ones in the cannabis plant, reaching "whole plant" or "full spectrum" composition is not necessarily an advantage. For enhanced therapeutic

effects, desired compositions are attainable by enriching extracts with selected terpenes. These compositions adjust the treatment for various desired medicinal and personal needs.

Reference:

Selected Cannabis Terpenes Synergize with THC to produce increased CB1 Receptor activation;

<https://www.sciencedirect.com/science/article/pii/S0006295223001399?via%3Dihub>

<<https://dim.mcusercontent.com/cs/fd0e56ff0828ad1078ee6b45e/images/70b9532b-ec75-d00e-087d-546541a5f426.jpeg?w=564&dpr=2>>



Self-Dosing CBD Use Found To Decrease Drowsiness, Diabetes & Low Testosterone

As the number of people who use cannabidiol (CBD) increasingly rises, regulatory bodies, such as the FDA (Food and Drug Administration), are concerned about the use of CBD in adults. Data from studies can be used to understand better the effects of CBD on the liver, daytime drowsiness and testosterone levels and inform dosing protocols.

A recent clinical study platform was used to collect data from 1,061 adults who self-dose with CBD. Customers from US CBD brands were recruited via social media and sent a CBD product to use for the study. Participants provided personal information, medical history, reasons for taking CBD, present dosage, form and composition of CBD, alcohol consumption and current medications and

conditions. They reported the effects of the CBD over 30 days in a daily journal, after which blood samples were drawn and tested for liver tests and testosterone levels in men.

Most of the participants used full-spectrum CBD oil or CBD isolate. The average daily dose of CBD was 0.65 - 0.57 mg/kg/day, which is typical. The daily dose of CBD consumed by participants who used an oral, full-spectrum CBD product formulated using nanotechnology was significantly lower than that of CBD isolate and broad-spectrum CBD. 33 participants reported side effects, most of which were probably unrelated to CBD ingestion.

In this large-sample study, individuals self-dosing CBD had decreased daily drowsiness, decreased diabetes, and decreased low testosterone, and no participants demonstrated liver disease. In this study, older individuals taking CBD had a lower prevalence of low testosterone and a lower prevalence of type 2 diabetes than the general population. Clinical trials are needed to further assess the safety of CBD in adults.

Reference:

The Effects of Long-Term Self-Dosing of Cannabidiol on Drowsiness, Testosterone Levels, and Liver Function

<https://www.karger.com/Article/Abstract/529677>



The Directors of the Company accept responsibility for the contents of this announcement.

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About Ananda Developments

Ananda is an AQSE-listed medical cannabis company creating UK-based operations to grow and provide carbon zero, consistent, medical cannabis for the UK and international markets.

The UK medical cannabis market is predicted to be worth £450m by 2025 and the European market is predicted to be worth USD4.2bn by 2027.

For more information, please visit: <https://anadadevelopments.com/>

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