

ANANDA DEVELOPMENTS PLC

Cannabinoid Medicine Research Roundup

Issue Twenty-One

Ananda's ambition is to be a leading provider of high-quality cannabinoid medicines for the treatment of complex, chronic inflammatory pain conditions in the UK and for international markets.

Summary:

We have now renamed this document the Cannabinoid Medicine Research Roundup. Over time we are seeing research become more targeted into mechanisms, pathways and individual cannabinoids in the attempt to understand how cannabis and/or its constituents work – individually and together. As we continue to develop our pharmaceutical grade cannabinoid medicines and the evidence needed for the NHS and other countries' medical systems to prescribe them, we believe that it is important to frame the conversation in the appropriate terms.

Since our last issue in June 2023 we have seen papers dealing with *in vitro*, *in vivo* and clinical evidence in areas as wide-ranging as the positive activity of the Endocannabinoid System and/or cannabidiol (CBD) in the clinic in untreated hypertension and *in vivo* of axon regeneration following injury, more evidence in epilepsy, and an *in vitro* acne model demonstrating the positive effect of CBD. See links to these articles at the bottom of this issue.

For this edition we have summarised three particularly interesting articles in further detail. If you are taking tamoxifen or know someone with sickle cell disease then you should be particularly interested. We also look at the role of CBD in aging – as if the rest of CBD's activities were not enough... it just might help you live longer!

CBD-oil as a potential solution in case of severe tamoxifen-related side effects

<https://www.nature.com/articles/s41523-023-00570-x>

Tamoxifen is effective in the treatment of estrogen-receptor positive breast cancer and is recommended for two to three years for postmenopausal patients and up to ten years for premenopausal patients.

Unfortunately, tamoxifen can lead to bothersome side effects such as hot flashes, arthralgia, insomnia, and mood alterations. Forty percent of patients eventually discontinue tamoxifen therapy early, mainly due to side effects.

In this open label trial of 26 patients taking tamoxifen and tamoxifen + CBD, over 50 percent of the patients saw an improvement in the side effect symptoms compared to baseline.

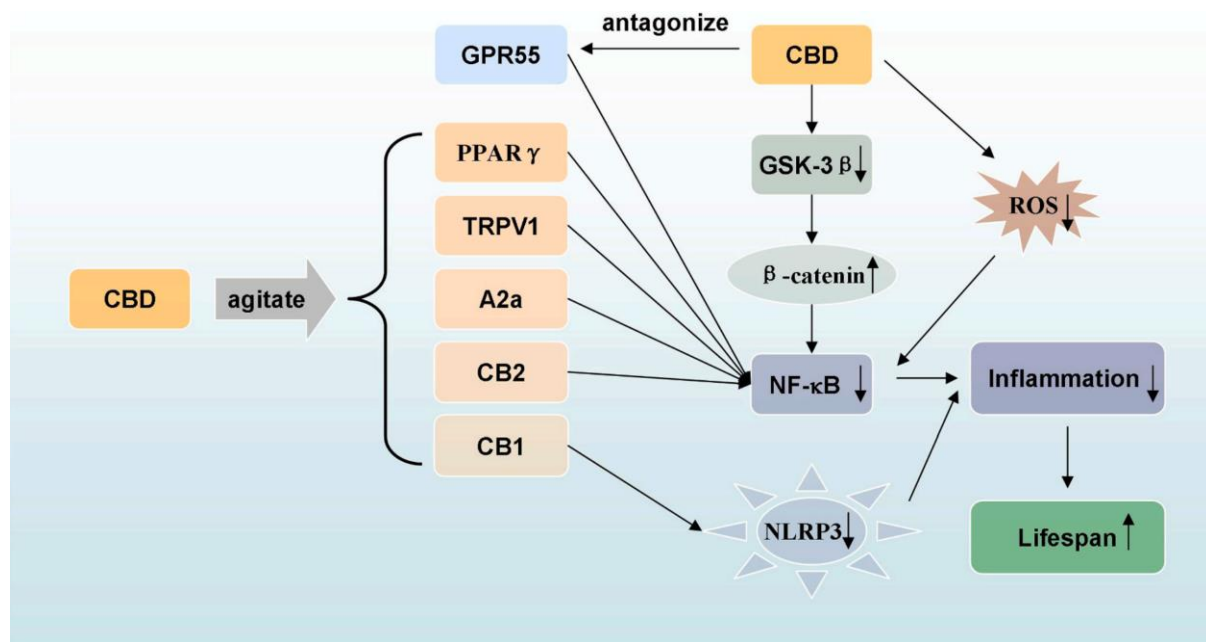
The most common side effects which was also where most of the improvement was included hot flashes, joint pain, insomnia, sweats and mood swings.

The role of CBD in aging

<https://www.sciencedirect.com/science/article/pii/S075333222300865X>

Aging is a very complex biological process. Current research shows that there are at least 14 cellular and molecular hallmarks of aging: deregulated nutrient sensing, mitochondrial dysfunction, cellular senescence, compromised autophagy, inflammation, disturbance of the microbiome, etc.

Multiple biological processes are involved in aging, such as oxidative stress, inflammation, autophagy, proteostasis, cellular senescence and DNA damage. Here, this article highlighted the particular effect of CBD on oxidative stress, inflammation and autophagy and clarified its antiaging mechanism.



CBD changed the life of this boy with sickle cell disease

<https://onlinelibrary.wiley.com/doi/10.1002/ajh.27049>

Patients with sickle cell disease (SCD) suffer from both acute and chronic pain, whose pathophysiology involves not only red blood cell sickling with subsequent vaso-occlusion leading to ischemia reperfusion injury, but also neurogenic inflammation, possibly mediated by mast cell activation.

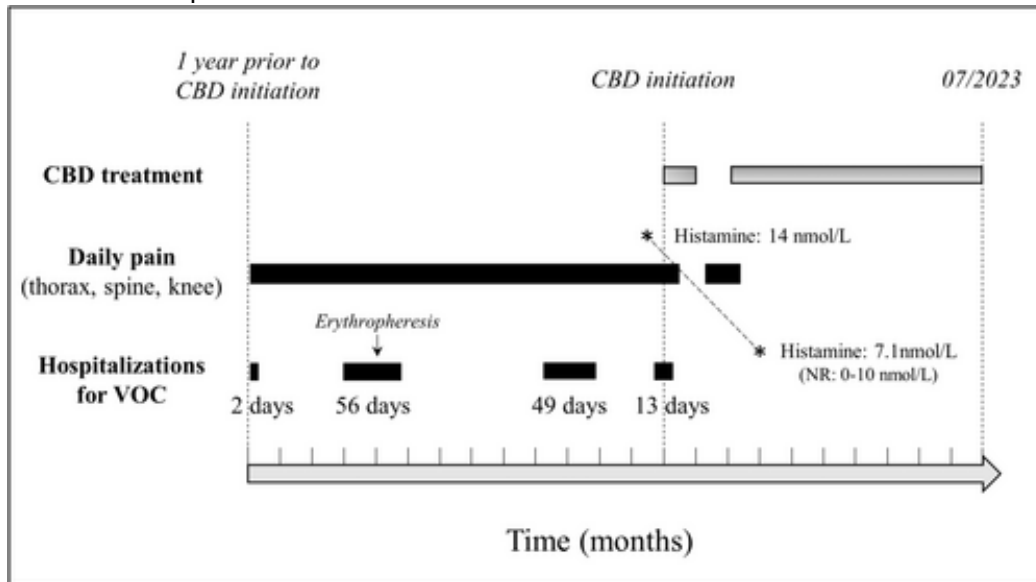
Chronic pain affects approximately 40 percent of patients with SCD, and its management is often a difficult challenge for clinicians. Indeed, morphine, which has long been considered the reference analgesic for acute pain, may paradoxically worsen chronic pain, by promoting mast cell activation and degranulation, leading to the release of mast cell mediators such as substance P or histamine.

This 15-year-old man with SCD had a history of 5 to 10 hospitalisations per year – two of these were for 56 and 49 days because of the inefficacy of conventional analgesics, including intravenous paracetamol, nalbuphine, morphine (PCA), nefopam, ketamine, and amitriptyline.

The patient suffered from daily chronic pain in the lumbar spine, thorax, and right knee, described as intense and permanent with overlying cutaneous hyperesthesia and intermittent tingling sensation. He was later started at 3 mg/kg of CBD per day gradually increasing over a month to 22 mg/kg/day in 3 doses.

Two weeks were enough to observe a complete regression of pain in the lumbar spine, thorax, and right knee. The patient discontinued CBD one month after introduction due to supply disruption, which caused recurrence of pain in the lumbar spine, thorax, and right knee after one week.

Resumption of treatment at the same dose allowed further regression of pain within one week. Since the beginning of CBD treatment, the patient has not required further hospitalization for VOC, with a follow-up of 10 months.



Additional articles

The Influence of Oral Cannabidiol on 24-h Ambulatory Blood Pressure and Arterial Stiffness in Untreated Hypertension: A Double-Blind, Placebo-Controlled, Cross-Over Pilot Study
<https://link.springer.com/article/10.1007/s12325-023-02560-8>

Injury-induced activation of the endocannabinoid system promotes axon regeneration
[https://www.cell.com/iscience/fulltext/S2589-0042\(23\)00891-X?returnURL=https%3A%2F%2Flinkinghub.elsevier.com%2Fretrieve%2Fpii%2FS258900422300891X%3Fshowall%3Dtrue](https://www.cell.com/iscience/fulltext/S2589-0042(23)00891-X?returnURL=https%3A%2F%2Flinkinghub.elsevier.com%2Fretrieve%2Fpii%2FS258900422300891X%3Fshowall%3Dtrue)

Real-world experience with cannabidiol as add-on treatment in drug-resistant epilepsy
[https://www.seizure-journal.com/article/S1059-1311\(23\)00193-0/fulltext](https://www.seizure-journal.com/article/S1059-1311(23)00193-0/fulltext)

In vitro acne disease model from inertial focusing effect for studying the interactions between sebocyte glands and macrophages.
<https://europepmc.org/article/med/37477791>

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 company whose ambition is to be a leading provider of cannabinoid-based medicines for the treatment of complex, chronic inflammatory pain conditions.

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