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PEA: ENDOCANNABINOÏDE D'INTÉRÊT VÉTÉRINAIRE





Invitation Webinaire

◦ Arnaud Darnis : introduction


- welcome - agenda
- 2 min



Dr. Thierry Poitte



Dr. Agnès Darnis



Lundi 20 novembre 2023 19h - 20h
50 minutes de présentation et 10 minutes de questions-réponses

QUALITÉ ET CONFORT DE VIE: CAS PRATIQUES AUTOUR DU PEA, UN ENDOCANNABINOÏDE D'INTÉRÊT VÉTÉRINAIRE.

- Public visé : vétérinaires
- Programme
- Le PEA, que sait-on en 2023 ?
- Mode d'action
- Cas de la littérature sur différents usages vétérinaires
- Nouveautés en médecine humaine

Expériences cliniques avec le PEA en pratique vétérinaire

- Utilisation du PEA seul
- Utilisation du PEA en approche multimodale

• Intervenants :

Dr Thierry Poitte : DVM, Fondateur de CAPDouleur
Dr Agnès Darnis : DVM, Vêtozen


• Inscriptions : scannez le QR Code ci-contre ou saisissez le lien d'inscription suivant pour le direct ou le replay : [https://us02web.zoom.us/join/register/WN_BXyoOci1ST5Yio0GkXiQA#/
 registration](https://us02web.zoom.us/join/register/WN_BXyoOci1ST5Yio0GkXiQA#/)

Webinaire


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PEA: ENDOCANNABINOÏDE D'INTÉRÊT VÉTÉRINAIRE




1° Le PEA, que sait-on en 2023 ?

- Mode d'action
- Revue bibliographique
- Nouveautés en médecine humaine


2° Expériences cliniques avec le PEA en pratique vétérinaire

- Utilisation du PEA seul
- Utilisation du PEA en approche multimodale


Conclusion: Perspectives et usages du PEA versus CBD


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PEA: ENDOCANNABINOÏDE D'INTÉRÊT VÉTÉRINAIRE



PEA: MODE D'ACTION

Amides d'acides gras ou fatty acid amides = FAA

CCCCCCCCCCCCCCCC(=O)NCCO

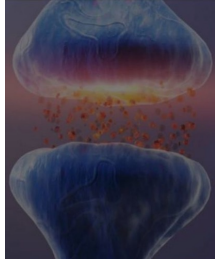
PEA = PALMITOYLETHANOLAMIDE

C18=CCCC=CCCC=CCCC(=O)NCCO


Anandamide

Parenté structurelle et fonctionnelle


Médiateur endocannabinoïde-like à actions anti-inflammatoire et analgésique (↑ hypersensibilité)




ALIAmides: famille d'amides d'acides gras à action Antagonisme Local de l'Inflammation Autacoïde (ALIA)


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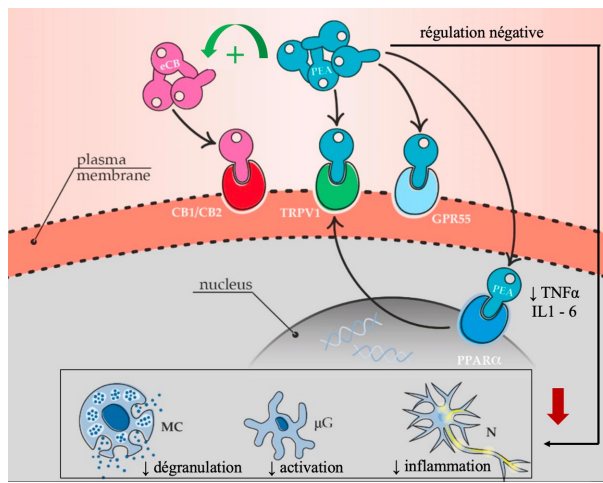
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PEA: ENDOCANNABINOÏDE D'INTÉRÊT VÉTÉRINAIRE



PEA: MODE D'ACTION




Della Rocca G, Gamba D. Chronic Pain in Dogs and Cats: Is There Place for Dietary Intervention with Micro-Palmitoylethanolamide? *Animals (Basel)*. 2021 Mar 29;11(4):952.

1° ↑ Endocannabinoïdes et action indirecte sur CB1 CB2

2° Fixation: SEC


- TRPV1
- GPR55
- PPARα

3° Effet ALIA:
Autacoïd Local Injury Antagonism
Autacoïdes antagonistes des lésions locales grec
autos (auto) et acos (soulagement)




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PEA: ENDOCANNABINOÏDE D'INTÉRÊT VÉTÉRINAIRE



PEA: MODE D'ACTION

1° ↑ Endocannabinoïdes et action indirecte sur CB1 CB2

INTERACTIONS AVEC LE SYSTÈME ENDOCANNABINOÏDE

Endocannabinoïdes

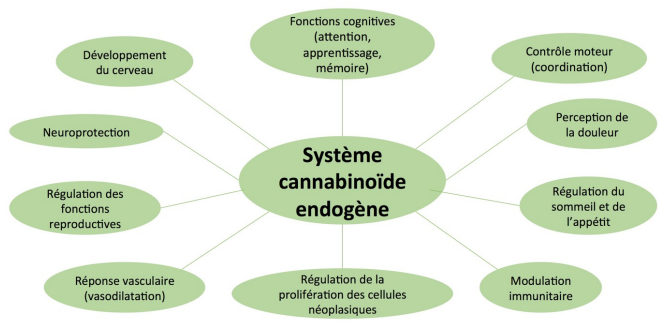
Anandamide (AEA)
2- arachidonoylglycerol (2-AG)
N-palmitoyl ethanolamide (PEA)
 Oleoylethanolamide OEA
 Homo linoleoyl ethanolamide
 Docosa tetranyl ethanolamide


Enzymes

➢ De dégradation et de synthèse
 "fatty acid amide hydrolase" FAAH

CB1	CB2	CB1 & CB2
gastro-intestinal testis brain liver muscle reproductive cellular vascular system	spleen spleen skin parts of the brain	skin spleen gall bladder bone marrow brain stem


Récepteurs





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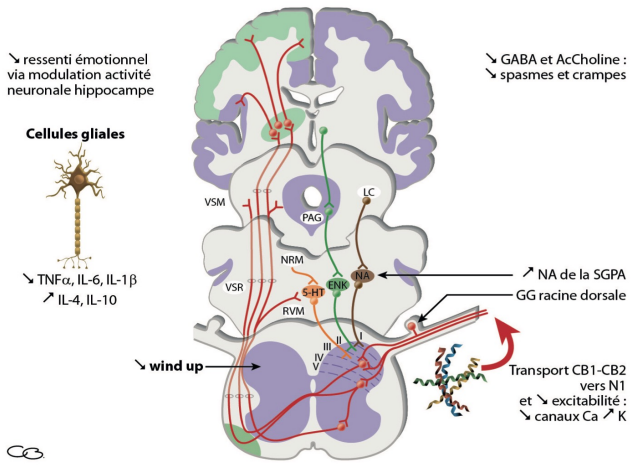



PEA: ENDOCANNABINOÏDE D'INTÉRÊT VÉTÉRINAIRE

PEA: MODE D'ACTION

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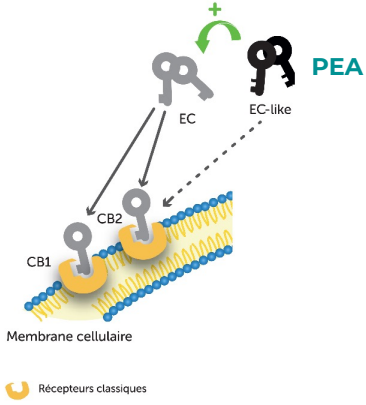
PEA: MODE D'ACTION


1° ↑ Endocannabinoïdes et action indirecte sur CB1 CB2



Les endocannabinoïdes (EC) :


- Anandamide (arachidonoyléthanolamide AEA) : agoniste complet du CB1 et partiel du CB2.
- 2-arachidonoylglycérol (2-AG) : agoniste complet du CB1 et du CB2.





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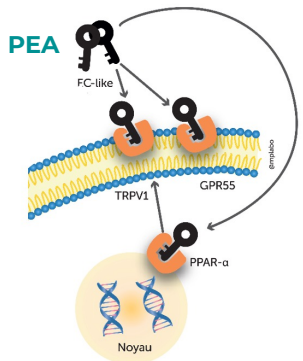


PEA: ENDOCANNABINOÏDE D'INTÉRÊT VÉTÉRINAIRE

PEA: MODE D'ACTION

2° Fixation: TRPV1 - GPR55 - PPARα






Récepteurs alternatifs


Récepteurs alternatifs EC-like :

- **Membranaires :** TRPV-1 (Transient Receptor Potential Vanilloïde), GPCR55, GPCR119.
- **Nucléaires :** PPAR-α (Peroxisome Proliferator-Activated Receptor alpha).



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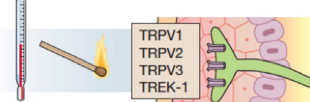
PEA: MODE D'ACTION

2° Fixation: TRPV1 - GPR55 - PPARα



TRPV1

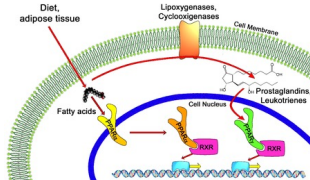
Transient Receptor Potential Vanilloïd 1



Rôle clé dans la nociception

PPARα

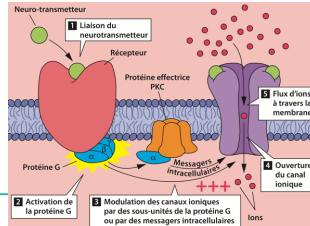
Récepteurs nucléaires activés par les proliférateurs de peroxisomes



Homéostasie lipidique et glucidique
Facteurs de transcription activant les gènes qui contrôlent la douleur et l'inflammation.


GPR55

Récepteurs membranaires couplés aux protéines G




Activation protéine G: 2nd messagers: AMPc - PKA et PKC

- ↑ signal nociceptif
- hypersensibilisation
- inscription dans la durée




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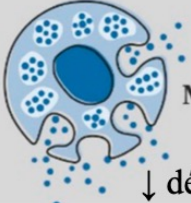


PEA: ENDOCANNABINOÏDE D'INTÉRÊT VÉTÉRINAIRE




PEA: MODE D'ACTION

3° Effet ALIA:
Autocoid Local Injury Antagonism = Autacoïdes antagonistes des lésions locales
 grec autos (auto) et acos (soulagement)



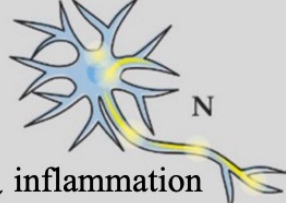
MC

↓ dégranulation



µG


↓ activation



N

↓ inflammation


Autacoïdes
 = facteurs de modulation produits localement à la demande
 influençant localement la fonction des cellules et / ou des tissus,
 et qui sont par la suite métabolisés dans les mêmes cellules et / ou tissus




Gugliandolo E et al. Palmitoylethanolamide and Related ALIAmides: Prohomeostatic Lipid Compounds for Animal Health and Wellbeing. Vet. Sci. 2020, 7, 78;

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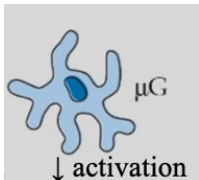
PEA: PERSPECTIVES D'UTILISATION

SOULAGEMENT DE LA DOULEUR ?

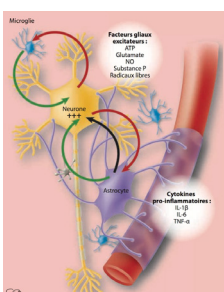
1° ≠ analgésique
 Pas de ↓ du seuil de la douleur physiologique des animaux ou de l'homme
 2° = antihyperalgésique ?

3° = antiinflammatoire

↓ Facteurs excitateurs gliaux:
Glutamate Cytokines




↓ activation



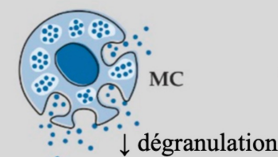
Facteurs gliaux excitateurs :
ATP
Glutamate
NO
Substance P
Radicaux libres

Cytokines pro-inflammatoires:
IL-1β
IL-6
TNF-α


Effets autacoïdes antagonistes des lésions locales



↓ inflammation




↓ dégranulation



*DiCesareMannelli, L et al. Delay of Morphine Tolerance by Palmitoylethanolamide. BioMed Res. Int. 2015, 894732.
 Luongo, L et al. Palmitoylethanolamide Reduces Formalin-Induced Neuropathic-like Behaviour through Spinal Glial/Microglial Phenotypical Changes in Mice. CNS Neurol. Disord. Drug Targets 2013, 12, 45-54*


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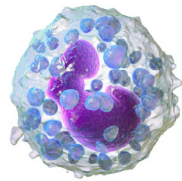
PEA: ENDOCANNABINOÏDE D'INTÉRÊT VÉTÉRINAIRE

PEA: MODE D'ACTION



SOULAGEMENT DE LA DOULEUR ?

1° ≠ analgésique
 Pas de ↓ du seuil de la douleur physiologique des animaux ou de l'homme
 2° = antihyperalgésique ?
 3° = antiinflammatoire




PEA **Effet ALIA**


Antagonisme Local de l'inflammation Autoçøide

- ↓ dégranulation des mastocytes
- ↓ libération de médiateurs pro-inflammatoires

1993: L'équipe de Rita Levi-Montalcini découvre le premier mécanisme in vivo sur les mastocytes



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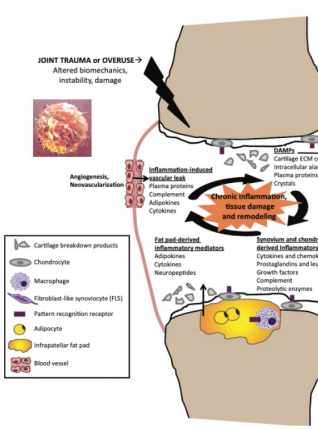
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PEA: PERSPECTIVES D'UTILISATION



Arthrose et inflammation

Mastocytes: orchestration inflammation (néovascularisation) ↑ VEGF et neuroinflammation ↑ NGF



Osteoarthritis and Cartilage

Osteoarthritis as an inflammatory disease (osteoarthritis is not osteoarthritis!)

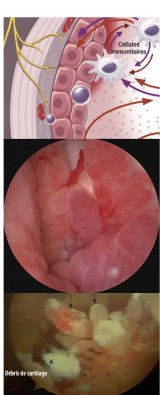
F. Beresbaum |¹

1. Department of Veterinary Medicine, University of California, Davis, California, USA; 2. Department of Veterinary Medicine, University of California, Davis, California, USA


Abstract

Osteoarthritis (OA) has long been considered a "wear and tear" disease resulting from cartilage degeneration. OA used to be considered the most common and most disabling chronic disease of the elderly, particularly in the particular joint (i.e., medial or weight-bearing joints). However, recent research has shown that OA is a complex, multifactorial disease involving both genetic and environmental factors. The underlying mechanisms are still unclear, but the disease is now understood to be a result of an imbalance between cartilage degradation and repair. Mastocytes, which are present in the joint, have been shown to play a role in OA pathogenesis. Mastocytes release various mediators, including histamine, tryptase, and chymase, which can contribute to cartilage degradation. Additionally, mastocytes are involved in the inflammatory response, leading to increased vascularization and neuroinflammation. This process is driven by factors such as VEGF and NGF. The presence of mastocytes in the joint is associated with increased pain and inflammation. Targeting mastocytes with PEA may help to reduce inflammation and pain in OA patients.


Keywords: Osteoarthritis, Mastocytes, Inflammation, VEGF, NGF, Pain.




Sokolove J, Lepus CM. Role of inflammation in the pathogenesis of osteoarthritis: latest findings and interpretations. *Therapeutic Advances in Musculoskeletal Disease*. 2013;5(2):77-94.


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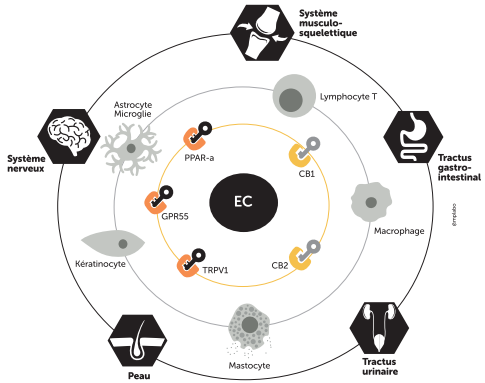
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PEA: PERSPECTIVES D'UTILISATION

AMÉLIORATION QUALITÉ DE VIE ?

ACTION PRO HOMÉOSTASIQUE DU PEA




Biomodulation naturelle par effet ALIA autoçoïde

- Action locale directe et indirecte sur:
 - Récepteurs
 - Différentes populations cellulaires
 - Organes

Les EC sont directement libérés des membranes cellulaires, ce qui les distingue d'autres messagers (neurotransmetteurs ou hormones) qui sont synthétisés à un endroit mais agissent globalement dans l'organisme.


Aloe, L.; Leon, A.; Levi-Montalcini, R. A proposed autocoid mechanism controlling mastocyte behaviour. Agents Actions 1993, 39, C145-C147.

Levi-Montalcini et al. A Nerve Growth Factor: From Neurotroph into Neurokine. Trends Neurosci. 1996, 19, 514-520.




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Available online at www.sciencedirect.com

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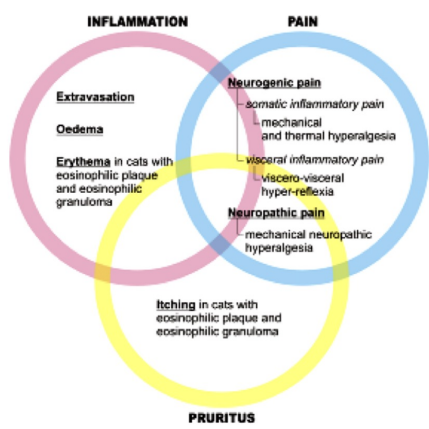
The Veterinary Journal 173 (2007) 21-30

Review

Palmitoylethanolamide, endocannabinoids and related cannabimimetic compounds in protection against tissue inflammation and pain: Potential use in companion animals


G. Re ^{a,*}, R. Barbero ^a, A. Miolo ^b, V. Di Marzo ^c

^a Department of Animal Pathology, Division of Pharmacology and Toxicology, Faculty of Veterinary Medicine, University of Turin, Via Leonardo da Vinci 44, I-10095 Grugliasco (TO), Italy
^b Scientific Information and Documentation Centre, Innovet Italia Srl, Viale Industria 8, I-35030 Rubano, Italy
^c Endocannabinoid Research Group, Institute of Biomolecular Chemistry, Consiglio Nazionale delle Ricerche, Via Campi Flegrei 34, I-80078 Pozzuoli, Napoli, Italy




The Veterinary Journal 173 (2007) 21-30

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2022

Palmitoylethanolamide and Related ALIAmides for Small Animal Health: State of the Art

Giorgia della Rocca^{1,2,3} and Giovanni Re¹

¹ Department of Veterinary Medicine, Centro di Ricerca e Diagnostics CARIEVA, University of Perugia, 06129 Perugia, Italy
² Department of Veterinary Sciences, Division of Pharmacology & Toxicology, University of Bari, 70126 Grottole, Italy
³ Comparative Geriatric/Neurogeriatrics

Abstract: ALIAmides are a family of fatty acid amides whose name comes from their mechanism of action, i.e., the Antinociceptive Lipid Antagonism (ALA). Actually, the ALIAmide parent molecule, palmitoylethanolamide (PEA), is locally produced (or obtained from a cell membrane precursor) in order to control immune-inflammatory cell responses, avert chronic pain resulting inflammation, and limit the resulting clinical signs. PEA-like ester compounds, with an additional and plant-terpene-derived chain mechanism of action with PEA and may also increase endogenous levels of PEA. Provided that their respective bioavailability is properly addressed (e.g., through decreasing the particle size through micellization), exogenously administered ALIAmides (that mimic, or sustain the pharmacological, functions of endogenous PEA, the aim of the present paper is to review the main findings on the use of ALIAmides in small animals as a vehicle to the aim of vision who has believed in the “according-to-nature” approach, namely Francesco della Valle. After briefly presenting some key issues on the molecular targets, metabolism, and pharmacokinetics of PEA and related ALIAmides, here we will focus on the preclinical and clinical studies performed in dogs and cats. Although more data are still needed, ALIAmides may represent a novel and promising approach to overall animal health.

Keywords: ALIAmides, dogs, cats, atopic dermatitis, osteoarthritis, mast cells, palmitoylethanolamide, Antinociceptive lipids/antagonism

Introduction
 ALIAmides are a family of fatty acid amides sharing a common mechanism of action, i.e., the antinociceptive lipid antagonism (ALA), originally proposed in the mid-1990s by the late Nobel prize winner Rita Levi Montalcini [1]. The term “antinociceptive” comes from the Greek “antice” (anti) and “nocice” (pain) and refers to self-produced factors that act locally near their site of synthesis [2]. In particular, the antinociceptive mechanism of ALIAmides involves anti-proliferative properties through the down-regulation of cell hyperactivity (mainly immune cells), thus controlling inflammatory responses and limiting tissue damage [3]. It was originally observed that the ALIAmide parent molecule, palmitoylethanolamide (PEA), down-modulates rat mast cell behavior after challenge [4], as later confirmed in comparative animals [5,7]. Different cell populations were also observed to be targets of PEA, with macrophages, leucocytes, T and B cells, and glial cells being respectively controlled by PEA once overactivated [6,11].

Palmitoylethanolamide is a body's own (endogenous) N-acyl-ethanolamine, produced “on demand” by several cell types, including mast cells, astrocytes, and microglia [7,11,12]. Interestingly, the antinociceptive function of PEA was first suggested in dogs. It was indeed revealed that (i) the canine myocardium produces PEA in response to thermal injury [12,13], and (ii) the canine brain possesses the biosynthetic and degradative machinery for PEA [14]. Since the 1990s, knowledge has advanced considerably in the field of ALIAmides, mainly

Veterinary Dermatology

Vet. Dermatol. 2015; 26: 432–e101 DOI: 10.1111/vde.12250

Efficacy of ultra-micronized palmitoylethanolamide in canine atopic dermatitis: an open-label multi-centre study


Chiara Noli^{*}, M. Federica della Valle[†], Alda Miolo[†], Cristina Medoriti[†], Carlo Schievano[‡] and The SkinItalia Clinical Research Group[†]

- Etude ouverte et multicentrique sur 160 chiens atteints de DAC.
- PEA 10 mg/kg SID
- Evaluations à J0 et J56: PVAS, CADLI, QoL
- ↓ Prurit
 - 58 % des chiens montrent une réduction de plus de 2 points
 - 30 % = pas de prurit
- ↓ CADLI
 - 62 % rémission (CADLI ≤5).
- QoL significativement améliorée




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2022

Palmitoylethanolamide and Related ALIAmides for Small Animal Health: State of the Art

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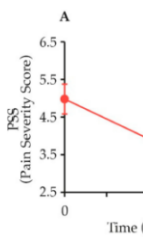
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Keywords: ALIAmides, dogs, cats, atopic dermatitis, osteoarthritis, mast cells, palmitoylethanolamide, Antinociceptive lipids/antagonism

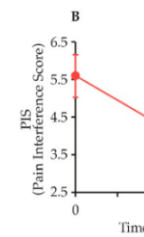
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↓ PSS et PSI CBPI




A
 PSS (Pain Severity Score)
 Time (week)




B
 PIS (Pain Interference Score)
 Time (week)

Figure 7. Dietary administration of PEA-q to privately owned dogs with chronic pain reduced the CBPI score. (A) During the four-week treatment, the mean severity of pain on PSS decreased significantly (*, $p = 0.023$). (B) The decrease of mean PIS was already statistically significant at the first control (week 2) and maintained a statistically significant decrease at the end of the study (week 4) (*, $p = 0.009$ for both comparisons). Drawn from data presented in [265].





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MÉDECINE HUMAINE

POST HOC ANALYSIS OF A CLINICAL TRIAL

Micronized Palmitoylethanolamide: A Post Hoc Analysis of a Controlled Study in Patients with Low Back Pain – Sciatica

Giorgio Cruccu¹, Giulia Di Stefano², Paolo Marchetti¹ and Andrea Truini¹

Department of Human Neuroscience, Sapienza University, Rome, Italy; ¹Pain Medicine Center of Scientific Institute H. San Raffaele in Milan, Milan, Italy

Abstract: Background: Despite being widely prescribed, relatively few controlled trials have been conducted on the class of neurotrophic/anticonvulsant neurocannabinoids. While performing a search in the literature, we came across an old registration study on micronized palmitoylethanolamide in patients with low back pain – sciatica (ClinicalTrials.gov).

Methods: We contacted the authors of the article and obtained all the original material, which allowed us to re-analyze the study. We assessed the clinical outcomes by calculating the numbers needed to treat for pain (visual analog scales) and function (Roland-Morris Questionnaire). After excluding patients for whom the experimental protocol was insufficient to respond and patients in case of the discontinuation of increasing probability of neuropathic pain (pain history, history with previous pain in ascending segments (e.g. phares or gait) changes with previous pain in the high or low back, sensory and ideomotority), and investigated any correlation (Spearman) between the improvement in pain and function with these two factors.

Results: Compared with placebo, palmitoylethanolamide 100 mg/day yielded a number needed to treat of 17.2 (95% confidence interval: 14.2) for pain, and 17.9 (95% confidence interval: 14.7) for function. The correlation between the two outcomes was highly significant for pain relief (P < 0.0005), although not significant for reduced dysfunction.

Conclusions: Palmitoylethanolamide was extremely effective on pain and function in a large cohort of patients with low back pain – sciatica. Although the multiple mechanisms of action of palmitoylethanolamide are still for mixed pain conditions such as low back pain – sciatica, the correlation between pain relief and the likelihood of neuropathic pain suggest that the drug acts as a modulator action on the neurotrophic pain component.

Keywords: Micronized palmitoylethanolamide, low back pain, neuropathic pain, mixed pain, neurocannabinoids, NSAIDs, placebo.

1. INTRODUCTION

Some neurocannabinoids considered to be effective in neuropathic and pain, such as alpha-lipoic acid, mexiletine, carbamazepine, and Palmitoylethanolamide (PEA), are supported by a large body of literature [1-7] though not by controlled trials, which are very limited in number.


Low back pain is a very common condition that causes medical disability and is a considerable socioeconomic burden [8, 9]. In the 2000s, people with low back pain during their lifetime [10]. Currently used pharmacological agents include Non-steroidal Anti-inflammatory Drugs (NSAIDs) and opioid analgesics, though both these classes of drugs have safety problems related to chronic treatment [11]. Despite the need for alternative treatment options with a better safety profile, the body of data available in the literature is still scarce [12]. We came across a registration study on micronized PEA (clinical trial ID: NCT00101010) conducted by Giulia and colleagues on a large cohort of patients with low back pain – sciatica [13]. In a condition of mixed neuropathic and nociceptive pain [14, 15]. This article had previously shown completely new features because the journal in which it had been published was not indexed by the main medical databases. We contacted the authors of the article and obtained all the original material, which allowed us to re-analyze the data and assess the clinical impact of the drug as well as its efficacy in neuropathic vs. nociceptive pain.

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Cohorte de 636 patients souffrant de lombalgie - sciatique.


PEA:
600 mg/jour, environ 10 mg/kg
“ extrêmement efficace pour soulager la sensation douloureuse
“ tendance à améliorer la fonction “




Gruccu G et al. Micronized Palmitoylethanolamide: A Post Hoc Analysis of a Controlled Study in Patients with Low Back Pain – Sciatica. CNS Neurol Disord Drug Targets. 2019 Aug; 18(6): 491–495.


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PEA: ENDOCANNABINOÏDE D'INTÉRÊT VÉTÉRINAIRE





MÉDECINE HUMAINE

Journal of Pain Research

Open Access Full Text Article

Therapeutic utility of palmitoylethanolamide in the treatment of neuropathic pain associated with various pathological conditions: a case series

This article was published in the following Dove Press journal: Journal of Pain Research 25 October 2012

Pain Physician 2016; 19:11-24 • ISSN 1533-3159

Systematic Review

Palmitoylethanolamide, a Special Food for Medical Purposes, in the Treatment of Chronic Pain: A Pooled Data Meta-analysis


Antonella Paladini, MD, PhD¹, Mariella Fusco, PhD², Teresa Cenacchi, MD, PhD³, Carlo Schievano, PhD⁴, Alba Pirolli, MD, PhD⁵, and Giustino Varrasi, MD, PhD⁶

Dovepress
open access to scientific and medical research

CASE SERIES


- ↓ douleur 40 à 80 % des cas (EN)
- entre 1^{ère} et 3^{ème} semaine
- polythérapie antalgique

- PEA: ↓ activation mastocytes et c. gliales
- score de douleur ≤ 3 chez 81% des patients traités par PEA
- Versus 40,9% chez les patients du groupe témoin après 60 jours de traitement.




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PEA: ENDOCANNABINOÏDE D'INTÉRÊT VÉTÉRINAIRE



MÉDECINE HUMAINE: TROUBLES COGNITIFS

Front Psychiatry, 2022; 13: 1038122.
Published online 2022 Oct 28. doi: [10.3389/fpsy.2022.1038122](https://doi.org/10.3389/fpsy.2022.1038122)

PMCID: PMC9650099
PMID: [36387000](https://pubmed.ncbi.nlm.nih.gov/36387000/)

Therapeutic effect of palmitoylethanolamide in cognitive decline: A systematic review and preliminary meta-analysis of preclinical and clinical evidence

[Marco Colizzi](#)^{1,2,*} [Riccardo Bortoletto](#)^{1,2,*} [Chiara Colli](#)^{1,*} [Enrico Bonomo](#)¹ [Daniele Pagliaro](#)¹ [Elisa Maso](#)¹
[Gianfranco Di Gennaro](#)³ and [Matteo Balestrieri](#)¹

Neurodégénérescence associée à dommages oxydatifs + neuroinflammation
+ dysfonction microvasculaire et de la barrière hémato-encéphalique.

↑ synthèse accrue de molécules de signalisation lipidique (dont PEA) en tant que tentative endogène pour:


- contrer ces mécanismes pathophysiologiques
- rétablir l'équilibre homéostatique

PEA améliore les fonctions neurocomportementales

- ↓ stress oxydatif
- ↓ activation microglie / β-amyloïde

Les preuves précliniques suggèrent que la PEA pourrait agir comme un médicament modifiant la maladie au stade précoce d'un trouble neurocognitif, tandis que son effet protecteur dans le trouble avéré peut être moins pertinent.

Objectif = réduire temporairement la gravité des symptômes



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PEA: PERSPECTIVES D'UTILISATION

AMÉLIORATION QUALITÉ DE VIE ? PEA ET TROUBLES COGNITIFS

Déficit des activités cognitives:
Syndrome Dysfonctionnement Cognitif
ou SDA: Syndrome de Dysfonctionnement lié à l'Âge
maladie neurodégénérative progressive des chiens et chats âgés résultant en une diminution de la fonction cérébrale supérieure

- déclin progressif des fonctions cognitives (l'ouïe, la mémoire, la perception et la conscience)
- changements dans les interactions sociales avec les humains, les animaux
- changements dans les habitudes de sommeil.

Prévalence: 14% à 22%
↑ avec l'âge: 41% > 14 ans
68% > 15 ans

↓ perception de l'environnement
↓ traitement des informations








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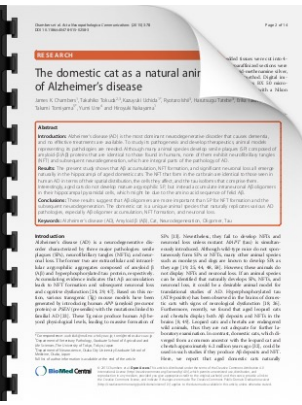



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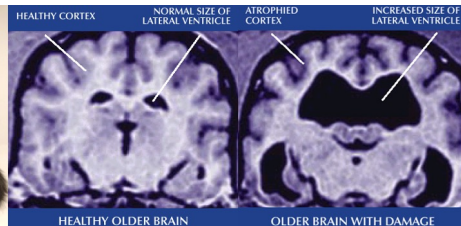
PEA: PERSPECTIVES D'UTILISATION

AMÉLIORATION QUALITÉ DE VIE ? PEA ET TROUBLES COGNITIFS










- Altération protéine tau: désorganisation de l'architecture neuronale + dégénérescence neurofibrillaire
- Dépôt de plaques amyloïdes génératrices de radicaux libres
- Les RL dégradent les lipides:
- Altération perméabilité membranaire et métabolisme cellulaire
- ↓ DHA



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PEA: PERSPECTIVES D'UTILISATION

AMÉLIORATION QUALITÉ DE VIE ? PEA ET TROUBLES COGNITIFS






Signes cliniques principaux du DCC		
Acronyme	Signification	Exemples
D	Disorientation (Désorientation)	- incapacité à trouver son chemin dans la maison ou autour d'objets - chien qui demeure immobile
I	Interaction (Interaction)	- réduction des interactions sociales - peur/irritabilité
S	Sleep (Sommeil)	- augmentation de l'activité nocturne - vocalisations nocturnes
H	Housetraining (Propreté/ Education)	- malpropreté dans la maison - incapacité d'apprendre de nouvelles commandes ou de répondre à des ordres connus
A	Activity (Activité)	- réduction de l'exploration/du jeu - errance - comportements répétitifs
A	Anxiety (Anxiété)	- augmentation de l'anxiété quand le chien est laissé seul - animal plus réactif/peureux

Benzal AS, Rodriguez AG. Recent developments in Canine Cognitive Dysfunction Syndrome. Pet Behaviour Science | 2016, Vol. 1, 47 - 59.



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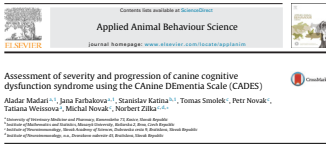


PEA: ENDOCANNABINOÏDE D'INTÉRÊT VÉTÉRINAIRE

PEA: PERSPECTIVES D'UTILISATION

AMÉLIORATION QUALITÉ DE VIE ? PEA ET TROUBLES COGNITIFS





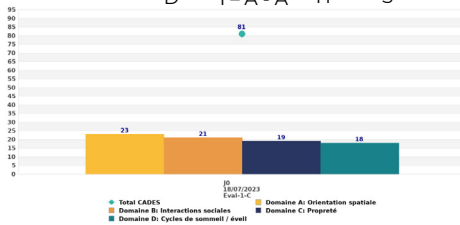
Assessment of severity and progression of canine cognitive dysfunction syndrome using the Canine Dementia Scale (CADES)
 Adar Madari¹, Jina Parkhaya¹, Sunita Kulkarni¹, Tomas Simcik¹, Petr Novak¹, Tatiana Weissova¹, Michal Novak¹, Norbert Zilka¹

Journal of Applied Animal Behaviour Science, Volume 1(1) (2023) 1-10


ABSTRACT
 Cognitive dysfunction syndrome (CDS) represents a group of symptoms observed in the aging often called dogs. These changes ultimately result in a decline of cognitive function and learning ability, decreased alertness, and memory impairment. Symptoms of CDS are characterized by a progressive decline in cognitive function. The latest symptoms gradually replace one over time. Single symptoms observed in 100% of cases about the age of 10 years, 90% at 12 years, 80% at 14 years, 70% at 16 years, 60% at 18 years, 50% at 20 years, 40% at 22 years, 30% at 24 years, 20% at 26 years, 10% at 28 years, and 0% at 30 years. The study has identified a total of 10 CDS-related clinical signs: disorientation, 11.1% of dogs; reduced alertness, 10.0%; reduced learning ability, 10.0%; reduced social interaction, 10.0%; reduced response to name, 10.0%; reduced response to touch, 10.0%; reduced response to sight, 10.0%; reduced response to sound, 10.0%; reduced response to smell, 10.0%; and reduced response to taste, 10.0%. The prevalence of CDS in 10-year-old dogs was 10.0%, 20.0% in 12-year-old dogs, 30.0% in 14-year-old dogs, 40.0% in 16-year-old dogs, 50.0% in 18-year-old dogs, 60.0% in 20-year-old dogs, 70.0% in 22-year-old dogs, 80.0% in 24-year-old dogs, 90.0% in 26-year-old dogs, and 100.0% in 28-year-old dogs. The prevalence of CDS in 10-year-old dogs was 10.0%, 20.0% in 12-year-old dogs, 30.0% in 14-year-old dogs, 40.0% in 16-year-old dogs, 50.0% in 18-year-old dogs, 60.0% in 20-year-old dogs, 70.0% in 22-year-old dogs, 80.0% in 24-year-old dogs, 90.0% in 26-year-old dogs, and 100.0% in 28-year-old dogs. The prevalence of CDS in 10-year-old dogs was 10.0%, 20.0% in 12-year-old dogs, 30.0% in 14-year-old dogs, 40.0% in 16-year-old dogs, 50.0% in 18-year-old dogs, 60.0% in 20-year-old dogs, 70.0% in 22-year-old dogs, 80.0% in 24-year-old dogs, 90.0% in 26-year-old dogs, and 100.0% in 28-year-old dogs.

SCORING CADES :
 Score 0-7 = Vieillesse normal
 Score 8-23 = Dysfonctionnement cognitif bénin
 Score 24-44 = Dysfonctionnement cognitif modéré
 Score 45-69 = Dysfonctionnement cognitif sévère
 Score 70-95 = Dysfonctionnement cognitif extrême

Jour	Date	Poids (Kg)	Composantes CADES				Score CADES
			A: Orientation spatiale	B: Interactions sociales	C: Propreté	D: Cycles de sommeil / éveil	
J0	18/07/2023	7	23/25	21/25	19/25	18/20	81




D I - A - A H S



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PEA: PERSPECTIVES D'UTILISATION


AMÉLIORATION QUALITÉ DE VIE ? PEA ET TROUBLES COGNITIFS



Drug and dose	Mechanism of action	DISHA categories improved	Drug and dose	Mechanism of action	DISHA categories improved
Selegiline ¹ 0.5-1mg/kg/24h (in the morning)	Selective and irreversible inhibitor of monoamine oxidase B. Improves the levels of catecholamines in the brain cortex, promotes free radical scavenging and protects nerves from degeneration	I-S-A	Phenobarbital ¹ 2.5-5mg/kg/12h	Enhancement of post-synaptic neuronal inhibition by increasing responsiveness to GABA	S and anxiety
Propentofylline ¹ 2.5-5mg/kg/12h	Methylxantine improves blood flow to the brain, inhibiting thrombus formation and reducing peripheral vascular resistance. It enhances nutrient input to brain cells and increases the production of adenosine, a fundamental nucleoside for mitochondrial metabolism	D-A	Diphenhydramine ² 2-4mg/kg/8-12h	Serotonin reuptake inhibitor	S
Nicergoline ² 0.25-0.5mg/kg/24h	Improves brain blood flow and activates cerebral metabolism. There are few studies about the effectiveness in the treatment of CCD.	A	Trazodone ² 2-5mg/kg as needed up to 8-10 mg/kg/8-12-24h	Serotonin 2A antagonist/ reuptake inhibitor	Anxiety
Adrafinil ² 20mg/kg/24h	Enhances the noradrenergic system	S-A	Diazepam ³ 0.5-2.2mg/kg/8-12h	All benzodiazepines potentiate the effects of GABA by increasing the affinity of the receptors for the neurotransmitter at the GABA-A receptors	S and anxiety
GABA ³ 30mg/kg/24h	Inhibitory neurotransmitter	S	Alprazolam ³ 0.02-0.1mg/kg/8-14h		
Gabapentin ² 10-30mg/kg/8-12h	Inhibition of the voltage-dependent calcium channels in the presynaptic membrane decreasing the release of excitatory neurotransmitters.	S	Oxazepam ³ 0.2-1.0 mg/kg/12-24h	Buspirone ⁴ 1mg/kg/24h	Selective serotonin agonist
N-acetyl-D-mannosamine ⁴ 250mg/dog/24h	An isomer and a precursor of sialic acids. These are the most abundant terminal monosaccharides on glycoconjugates on eukaryotic cell surfaces and are involved in a variety of cellular functions	D-S	Fluoxetine ⁵ 1mg/kg/24h	Selective serotonin reuptake inhibitor	I and anxiety

(1) Landsberg et al. 2012, (2) Dewey 2008, p. 126, (3) Inagawa et al. 2005, (4) Nagasawa et al. 2014


(1) De Risio and Platt 2014, p. 374, (2) Landsberg et al. 2013, p. 418, (3) Jaggy 2010, p. 488, (4) Jaggy 2010, p. 488, (5) Landsberg et al. 2013, p. 419




Landsberg, G.M., Nichol, J., and Araujo, J.A. 2012. Cognitive dysfunction syndrome. A disease of canine and feline brain aging. *Veterinary Clinics of North America-Small Animal Practice* 42: 749-768.

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animals

MDPI

Successful and Unsuccessful Brain Aging in Pets: Pathophysiological Mechanisms behind Clinical Signs and Potential Benefits from Palmitoylethanolamide Nutritional Intervention

Colin Scuderi^{1,2,3} and Lorenza Golini¹

1. Department of Pathology and Pharmacology "Umberto Sestini", Sapienza University of Rome, Via B. delle Uscie, 499, Rome, Italy; 2. Faculty of Veterinary Medicine, Department of Clinical Animal Surgery, Sapienza University of Rome, Via Salaria, 1316, Rome, Italy; 3. Department of Veterinary Pathology, Sapienza University of Rome, Via Salaria, 1316, Rome, Italy

Abstract Canine and feline cognitive dysfunction syndrome is a common neurodegenerative disorder of old age and a natural model of human Alzheimer's disease. With the amenable, long-term life expectancy and increasing number of old animals, it is of great importance to delay cognitive decline. Knowledge of cellular and molecular mechanisms underlying disease onset and progression is necessary to develop effective therapeutic approaches. Neuroinflammation, characterized by altered immune system activity by astrocytes, microglia, and mast cells, is commonly observed in aged and infirmed neurodegenerative states. This has prompted attention to find a way to modulate the altered immune system. In this context, great emphasis has been given to the role played by the endocannabinoid system. In animal models, treatment of the geriatric population with physiological and pathological neuroinflammation. Within the endocannabinoid system, gene expression has been found to be modulated by the use of a natural and safe cannabinoid. The availability of new cannabinoid formulations highly improved the oral bioavailability of palmitoylethanolamide, paving the way to its clinical use. The cannabinoid palmitoylethanolamide has been repeatedly tested in animal models of age-related neurodegeneration with promising results. Data accumulated so far suggest that supplementation with phytocannabinoid palmitoylethanolamide helps to accomplish both neuroinflammation and cognitive impairment in old animals.

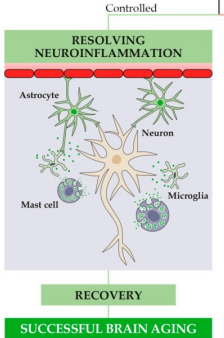
Keywords: Canine; feline; cognitive dysfunction syndrome; neuroinflammation; endocannabinoid system; palmitoylethanolamide

1. Introduction

Canine and feline cognitive dysfunction syndrome is a common neurodegenerative disorder of old age and a natural model of human Alzheimer's disease. With the amenable, long-term life expectancy and increasing number of old animals, it is of great importance to delay cognitive decline. Knowledge of cellular and molecular mechanisms underlying disease onset and progression is necessary to develop effective therapeutic approaches. Neuroinflammation, characterized by altered immune system activity by astrocytes, microglia, and mast cells, is commonly observed in aged and infirmed neurodegenerative states. This has prompted attention to find a way to modulate the altered immune system. In this context, great emphasis has been given to the role played by the endocannabinoid system. In animal models, treatment of the geriatric population with physiological and pathological neuroinflammation. Within the endocannabinoid system, gene expression has been found to be modulated by the use of a natural and safe cannabinoid. The availability of new cannabinoid formulations highly improved the oral bioavailability of palmitoylethanolamide, paving the way to its clinical use. The cannabinoid palmitoylethanolamide has been repeatedly tested in animal models of age-related neurodegeneration with promising results. Data accumulated so far suggest that supplementation with phytocannabinoid palmitoylethanolamide helps to accomplish both neuroinflammation and cognitive impairment in old animals.

Neurodégénérescence associée à **neuroinflammation** orchestrée dans le SNC par:

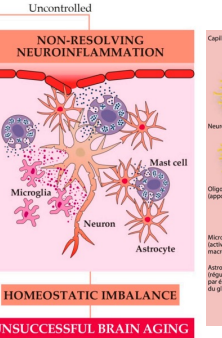
- Astrocytes + microglies: phénotype pro-excitateur
- Mastocytes résidents



RESOLVING NEUROINFLAMMATION

RECOVERY

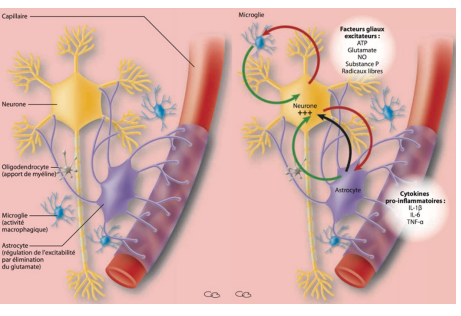
SUCCESSFUL BRAIN AGING



NON-RESOLVING NEUROINFLAMMATION


HOMEOSTATIC IMBALANCE

UNSUCCESSFUL BRAIN AGING




Scuderi C, Golini L. Successful and Unsuccessful Brain Aging in Pets: Pathophysiological Mechanisms behind Clinical Signs and Potential Benefits from Palmitoylethanolamide Nutritional Intervention. *Animals* 2021, 11, 2584. [h](https://doi.org/10.3390/ani11112584)

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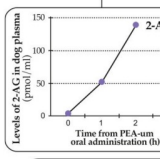


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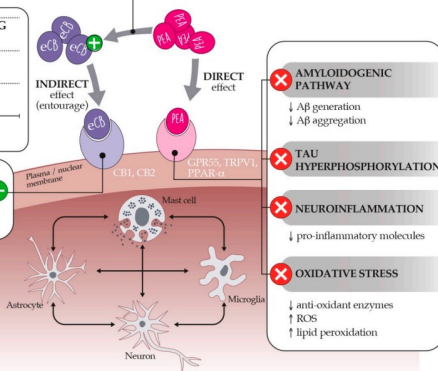
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AMÉLIORATION QUALITÉ DE VIE ? PEA ET TROUBLES COGNITIFS



MEMORY

- Stronger LTP



AMYLOIDGENIC PATHWAY

- ⊘ ↓ Aβ generation
- ⊘ ↓ Aβ aggregation

TAU HYPERPHOSPHORYLATION

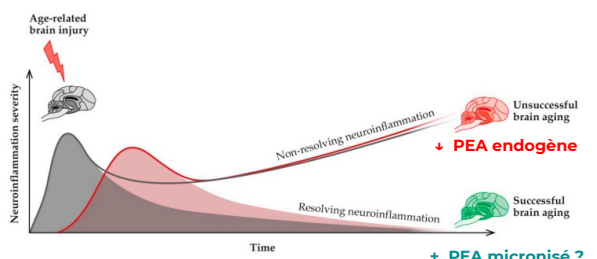
- ⊘

NEUROINFLAMMATION

- ⊘ ↓ pro-inflammatory molecules

OXIDATIVE STRESS

- ⊘ ↓ anti-oxidant enzymes
- ⊘ ↑ ROS
- ⊘ ↑ lipid peroxidation



Neuroinflammation severity

Time

Resolving neuroinflammation → Successful brain aging

Non-resolving neuroinflammation → Unsuccessful brain aging

↓ PEA endogène

+ PEA micronisé ?

Scuderi C, Golini L. Successful and Unsuccessful Brain Aging in Pets: Pathophysiological Mechanisms behind Clinical Signs and Potential Benefits from Palmitoylethanolamide Nutritional Intervention. *Animals* 2021, 11, 2584. [h](https://doi.org/10.3390/ani11112584)

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PEA: PERSPECTIVES D'UTILISATION



Palmidol® PEA
Confort et bien-être
Confort and well-being
30 gélules/capsules

PEA micronisé: ↑ biodisponibilité
100 mg / capsule



 10 mg/kg SID

 15 mg/kg SID

+ Astaxanthine
pigment
famille des xanthophylles (caroténoïdes)
algues séchées - krill
puissant antioxydant. 550 > Vit E




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◦ Cas clinique n°1 :

GAÏA



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PEA : ENDOCANNABINOÏDE D'INTÉRÊT VÉTÉRINAIRE

Cas clinique : boiterie

Commémoratifs

Border Collie femelle stérilisée, 12 ans


Score d'état corporel 6/9 : surpoids modéré

Boiterie antérieure gauche, évoluant depuis 15 mois

Difficultés à se lever après un temps de repos + boiterie 2/5 pendant 5-10 minutes



Boiterie jusqu'à 3/5 après 45-60 min de promenade, majorée la journée du lendemain

Examen orthopédique



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PEA : ENDOCANNABINOÏDE D'INTÉRÊT VÉTÉRINAIRE

Cas clinique : boiterie


Commémoratifs

Plan de traitement : Acupuncture : 3 séances à 3 semaines d'intervalle

Plan de traitement suite : Phytothérapie à visée anti-COX, LOX et métalloprotéases :


EPS Scrofulaire, Cassis, Mélilot : 4 semaines de traitement

Dans les 2 cas : rechute après 4-5 semaines après la fin du traitement




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PEA : ENDOCANNABINOÏDE D'INTÉRÊT VÉTÉRINAIRE




Cas clinique : boiterie


Commémoratifs

Bilan radiologique (F+ P, Coude et épaule) :

Composante arthrosique discrète, compatible avec son âge


Composante neuroinflammatoire combinée probable






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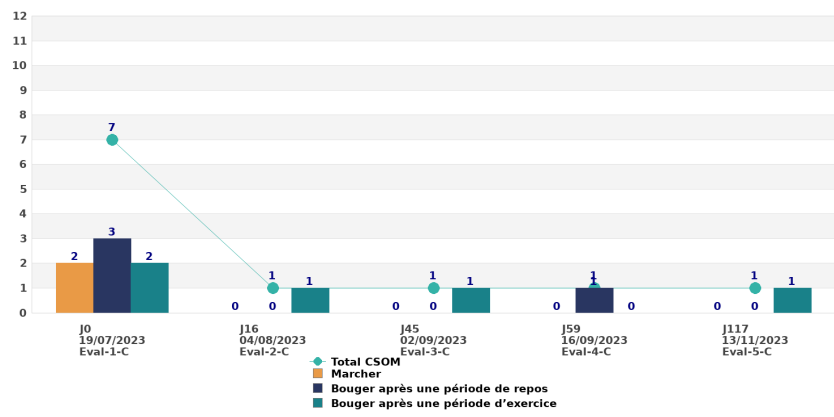
PEA: ENDOCANNABINOÏDE D'INTÉRÊT VÉTÉRINAIRE




Cas clinique : boiterie

Plan de traitement

- PEA en monothérapie 60 jours 300mg SID (le matin)
- **Suivi CSOM sur 4 mois**
- Score d'état corporel de 5/9 : poids idéal



Date	Marcher	Bouger après une période de repos	Bouger après une période d'exercice	Total CSOM
J0 19/07/2023 Eval-1-C	2	3	2	7
J16 04/08/2023 Eval-2-C	0	0	1	1
J45 02/09/2023 Eval-3-C	0	0	1	1
J59 16/09/2023 Eval-4-C	0	1	0	1
J117 13/11/2023 Eval-5-C	0	0	1	1



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 **WT-B**
COF




PEA: ENDOCANNABINOÏDE D'INTÉRÊT VÉTÉRINAIRE


◦ Cas clinique n°2:

CHANEL



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 **WT-B**
COF



PEA : ENDOCANNABINOÏDE D'INTÉRÊT VÉTÉRINAIRE

Cas clinique n°2

Commémoratifs


Chat européen femelle

Stérilisée, 6 ans

Vit en maison, avec accès à l'extérieur
Bonne entente avec les 2 chiens de la maison

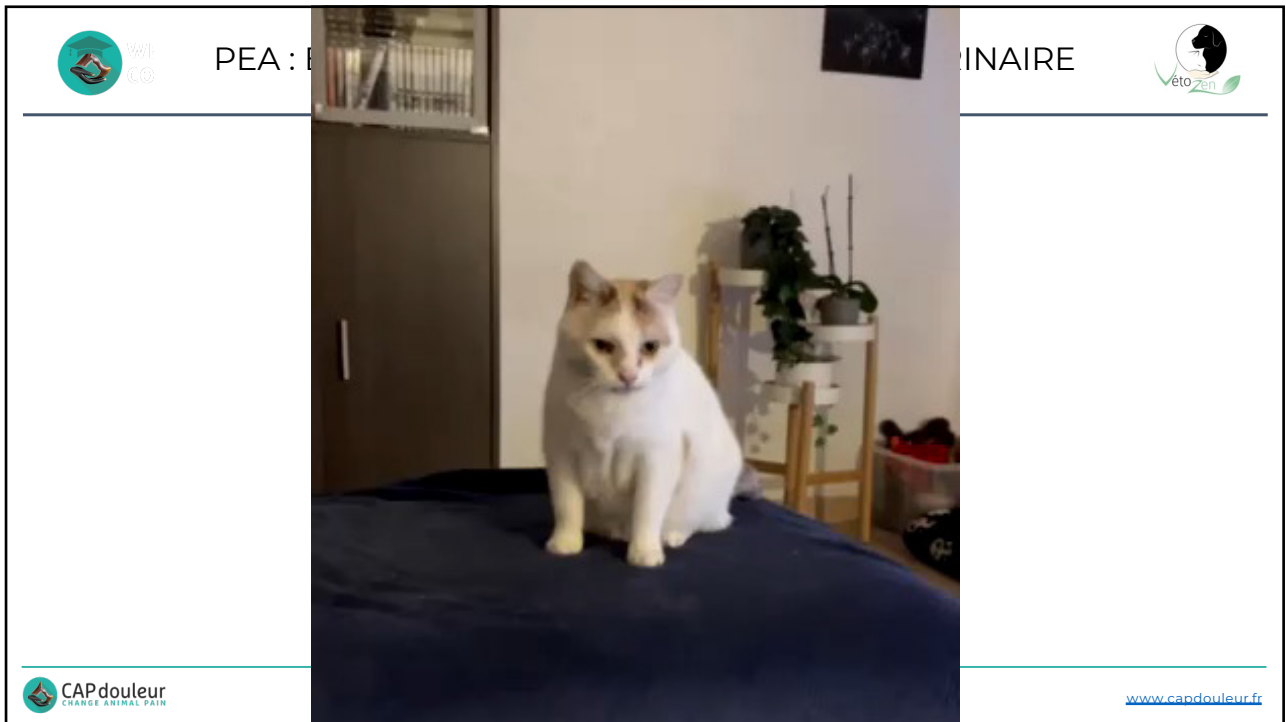
« Crises » depuis 8 à 10 mois

Quotidiennes depuis 2 mois (20-30 minutes)

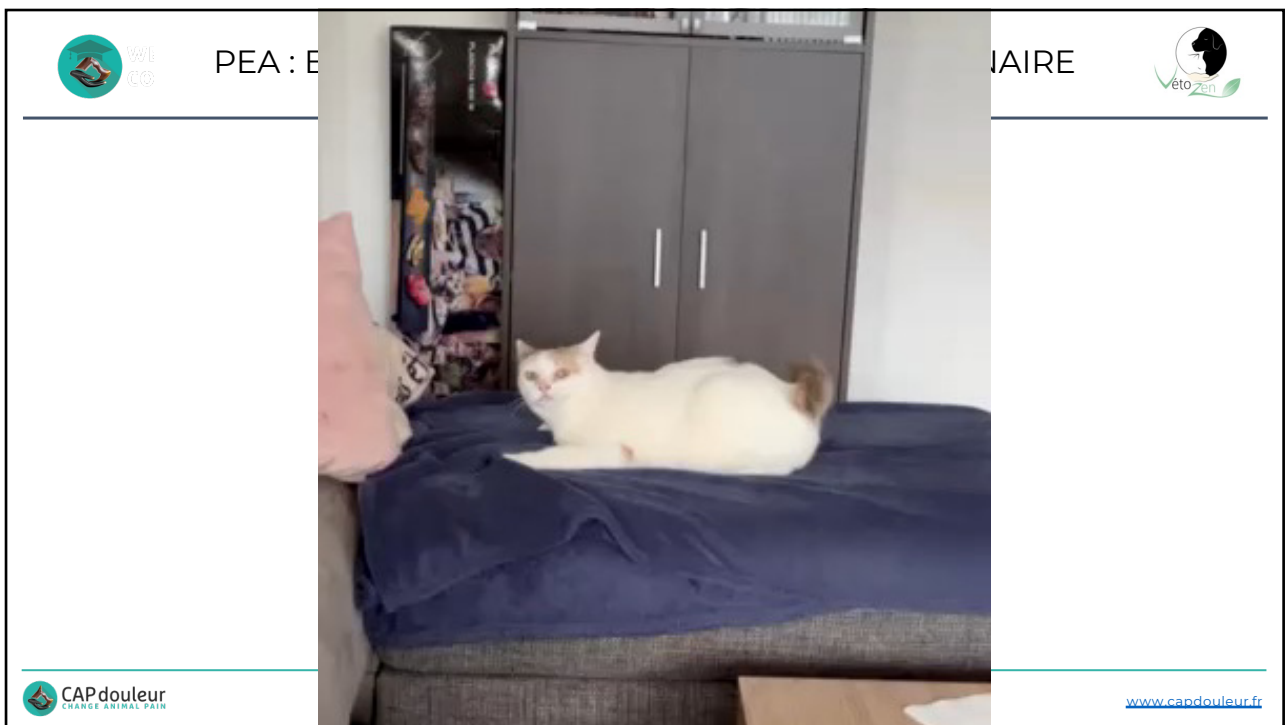
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PEA : ENDOCANNABINOÏDE D'INTÉRÊT VÉTÉRINAIRE



Cas clinique : Syndrome d'Hyperesthésie Féline


Commémoratifs

Syndrome d'Hyperesthésie Féline :


- Léchage compulsif localisé
- Mouvements saccadés langue et oreilles
- Rolling Skin Syndrom
- Agitation majeure, avec bonds

- Malpropreté urinaire fréquente (1 seul bac à litière couvert)


- Pas d'atteinte des relations sociales
- Pas d'automutilation


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PEA : ENDOCANNABINOÏDE D'INTÉRÊT VÉTÉRINAIRE



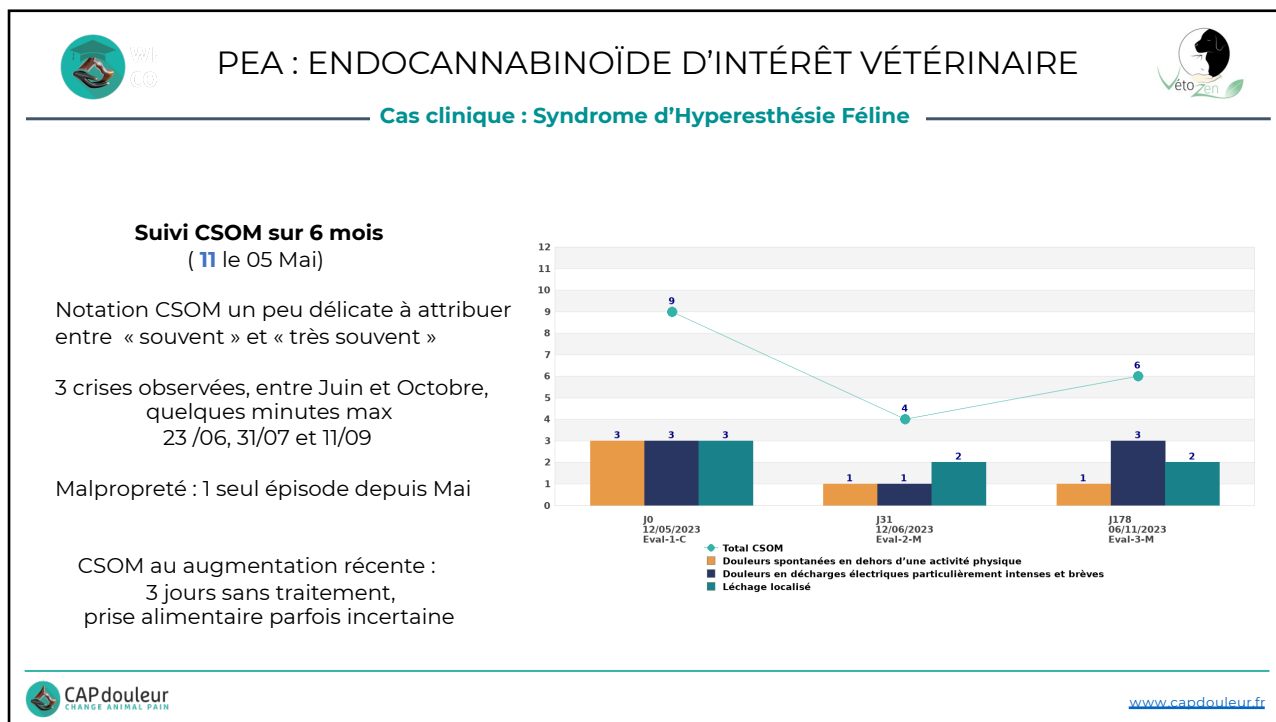
Cas clinique : Syndrome d'Hyperesthésie Féline

Plan de traitement

- Acupuncture, 1 séance 05 Mai : Sensibilité marquée des premières vertèbres caudales
- Mise en place d'un second bac à litière ouvert et de grande taille
- PEA : 100mg SID (le matin)


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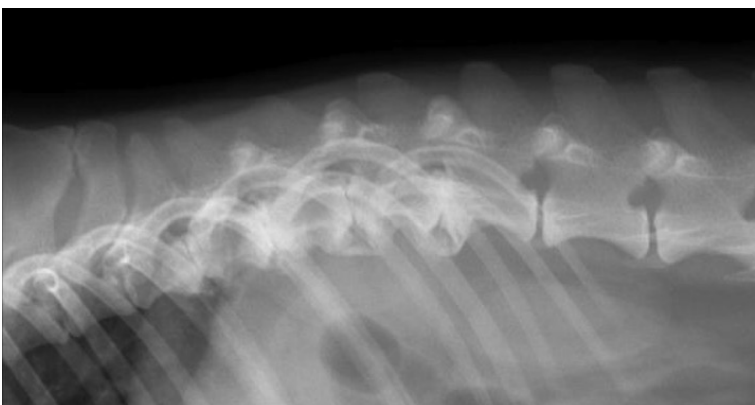



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PEA: ENDOCANNABINOÏDE D'INTÉRÊT VÉTÉRINAIRE








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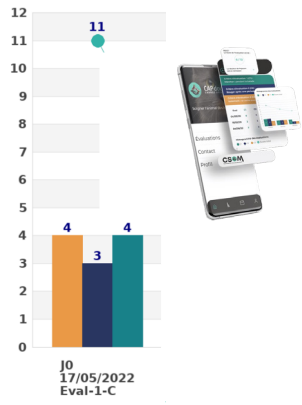


PEA: ENDOCANNABINOÏDE D'INTÉRÊT VÉTÉRINAIRE



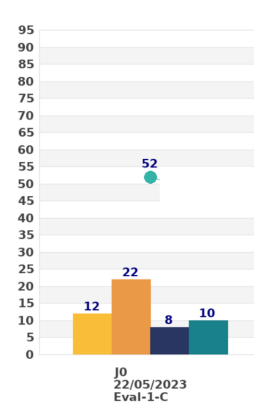
ÉVALUATION DOULEUR: CSOM

ÉVALUATION SDC: CADES



J0
17/05/2022
Eval-1-C


- ◆ Total CSOM
- Sauter
- Douleurs en décharges électriques particulièrement intenses et brèves
- Réaction douloureuse inédite au toucher ou à un évènement non douloureux (allodynie)



J0
22/05/2023
Eval-1-C

Jour	Date	Poids (Kg)	Composantes CADES				Score CADES
			A. Orientation spatiale	B. Interactions sociales	C. Propriété	D. Cycles de sommeil/éveil	
J0	22/05/2023	5	12/25	22/25	8/25	10/20	52

SCORING CADES :
 Score 0-7 = Vieillesse normale
 Score 8-23 = Dysfonctionnement cognitif bénin
 Score 24-44 = Dysfonctionnement cognitif modéré
Score 45-69 = Dysfonctionnement cognitif sévère
 Score 70-95 = Dysfonctionnement cognitif extrême


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PEA: ENDOCANNABINOÏDE D'INTÉRÊT VÉTÉRINAIRE




Eden Caniche M 4,3 kg 06/03/2009 5,1kg
CD: 17/05/2022 14 ans




- Bedinvetmab 5mg SC
- Gabapentine 20mg BID
- PEA Palmidol 100mg SID


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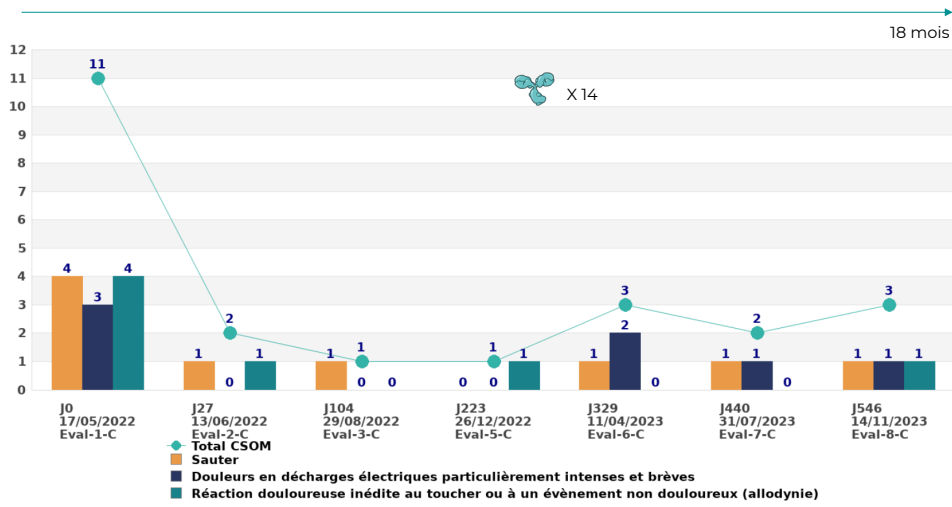
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PEA: ENDOCANNABINOÏDE D'INTÉRÊT VÉTÉRINAIRE



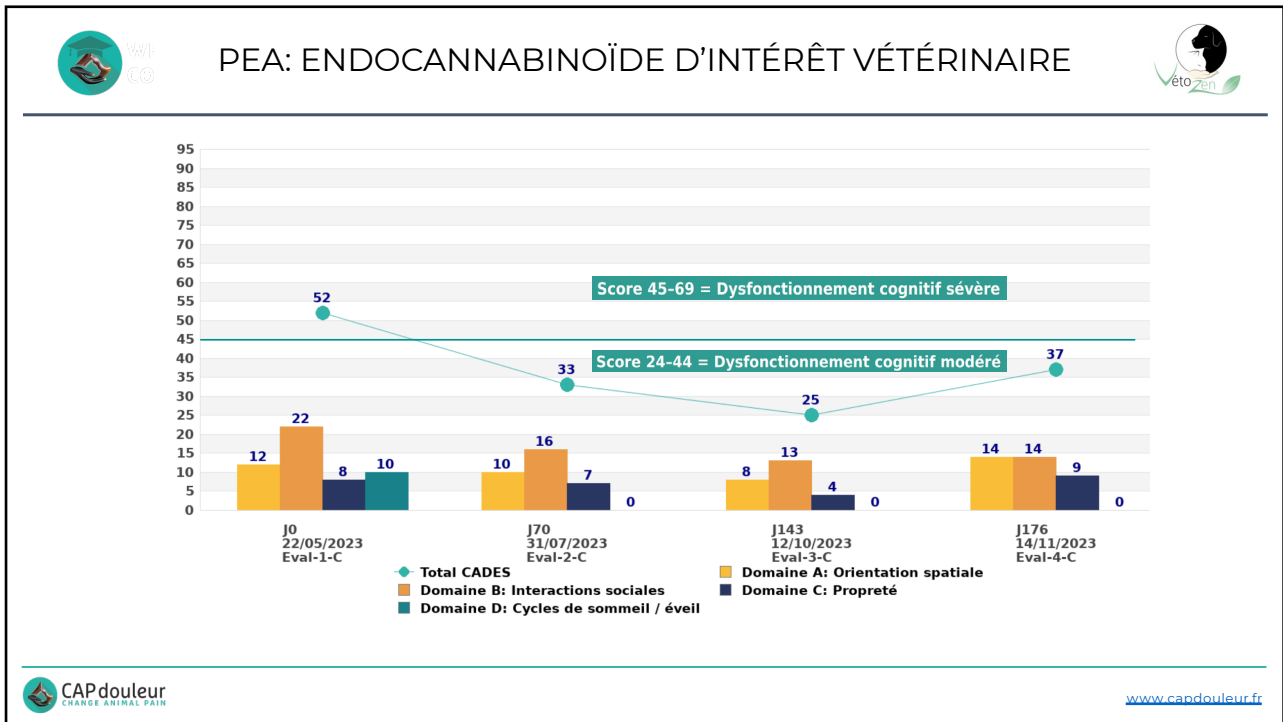
18 mois



Date	Eval	Total CSOM	Sauter	Douleurs en décharges électriques particulièrement intenses et brèves	Réaction douloureuse inédite au toucher ou à un événement non douloureux (allodynie)
J0	17/05/2022 Eval-1-C	11	4	3	4
J27	13/06/2022 Eval-2-C	2	1	0	1
J104	29/08/2022 Eval-3-C	1	1	0	0
J223	26/12/2022 Eval-5-C	1	0	0	1
J329	11/04/2023 Eval-6-C	3	1	2	0
J440	31/07/2023 Eval-7-C	2	1	1	0
J546	14/11/2023 Eval-8-C	3	1	1	1


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PERSPECTIVES ET USAGES VERSUS CBD

CC1=C(C(=C(C=C1)O)OC(=O)C2=CC=CC=C2)C


CBD

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PEA: ENDOCANNABINOÏDE D'INTÉRÊT VÉTÉRINAIRE



LIMITES D'UTILISATION DES PHYTOCANNABINOÏDES


EDITORIAL

Cannabis pour les douleurs ostéoarticulaires : un véritable espoir ou un simple effet de mode ?
Cannabis for osteoarticular pain: a real hope or a simple fashion effect?



Dr Serge Perrot
Omnipraticien, Département de Médecine, Paris Lodron 197, avenue de la République

Le cannabis thérapeutique contre la douleur : mirage plutôt que miracle ? - 19/08/23
Therapeutic cannabis for pain relief: A mirage rather than a miracle?
DOI: 10.1016/j.doa.2023.06.001
Marc Lévêque
Clinique Bouchard et hôpital privé Clairval, Marseille, France



crédit Anna Marin

larevuedupraticien

Cécile Manole ou Dr Marc Lévêque

Cannabis thérapeutique : beaucoup de bruit pour rien ?

Marc Lévêque¹, Laura Martin Aguiar² • **Affiliations et déclarations d'intérêt**


Publié le 24 novembre 2023

L'expérimentation du cannabis thérapeutique – qui vient d'être prolongée d'un an dans le PLUSS 2023 – suscite de l'espoir chez de nombreux patients souffrant de douleurs chroniques. Malheureusement, les résultats ne sont pas à la hauteur de ces attentes et, de facto, elle ouvre une brèche qui profitera surtout aux intérêts des industriels... Le point de vue du Dr Marc Lévêque, neurochirurgien spécialiste de la douleur.

Le projet de loi de financement de la Sécurité sociale (PLFSS) pour 2023, adopté par l'Assemblée nationale le 21 octobre puis le 15 novembre en **annexe lecture sur le Sénat**, prévoit la prolongation d'un an de l'expérimentation sur le cannabis thérapeutique.

Lancée en 2021, cette expérimentation menée sous l'égide de l'ANSM devait inclure 3 000 patients dans **Sindications précises** : douleurs neuropathiques réfractaires aux thérapies accessibles (médicamenteuses ou non) ; certains formes d'épilepsie sévères et pharmacorésistantes ; certains symptômes rebelles en oncologie liés au cancer ou à ses traitements ; situations palliatives ; spasticité douloureuse de la sclérose en plaques (SEP) ou des autres pathologies du système nerveux central.

Toutefois, seule la moitié des patients environ, sur les 3 000 initialement prévus, aurait été incluse (au 31 mars 2022) : « Les résultats sont insuffisants en termes de patients pour l'instant, pour avoir des résultats qui sont solides », **déclarait le ministre** de la Santé François Braun fin septembre à l'Assemblée – ce qui a motivé le prolongement de l'expérimentation. Le rapport d'évaluation, quant à lui, n'a pas encore été rendu public.



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DE VRAIES POTENTIALITÉS

Propriétés anxiolytiques
Homme et modèles animaux (rats et souris)
Implication du système sérotoninergique





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DE VRAIES POTENTIALITÉS

Propriétés anxiolytiques
 Homme et modèles animaux (rats et souris)
 Implication du système sérotoninergique



Propriétés myorelaxantes

- Spasticité de la Sclérose en Plaques
- Tremblements de la Maladie de Parkinson
- Myoclonies, contractures musculaires, RSS ...





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PEA: ENDOCANNABINOÏDE D'INTÉRÊT VÉTÉRINAIRE



CBD: DE VRAIES POTENTIALITÉS

Propriétés anxiolytiques
 Homme et modèles animaux (rats et souris)
 Implication du système sérotoninergique



Propriétés myorelaxantes

- Spasticité de la Sclérose en Plaques
- Tremblements de la Maladie de Parkinson
- Myoclonies, contractures musculaires, RSS ...




Propriétés antalgiques ?
 Douleurs neuropathiques > inflammatoires ??





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PEA: ENDOCANNABINOÏDE D'INTÉRÊT VÉTÉRINAIRE



LIMITES D'UTILISATION DES PHYTOCANNABINOÏDES


Pharmacocinétique



BIODISPONIBILITÉ
1^{er} passage hépatique

PHYTOTHÉRAPIE

- o Millepertuis + ISRS
= Syndrome sérotoninergique
- o CBD + ISRS
- o CBD + BZD





Métabolisme Phase I = oxydation / cytochromes

Inhibiteurs CYP450	fluconazole, kétoconazole, amiodarone, ciprofloxacine, clarithromycine, érythromycine, antidépresseurs tricycliques
Principaux médicaments menant à un surdosage	
Inducteurs CYP450	dexaméthasone, phénobarbital, rifampicine, phénytoïn, carbamazépine, spironolactone,
Principaux médicaments menant à un sousdosage	



INTERACTIONS MÉDICAMENTEUSES
 CBD: puissant inhibiteur cytochrome P450
 † concentrations sériques BZD – inhibiteurs calciques – ISRS AD3C - Opioides


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PEA: ENDOCANNABINOÏDE D'INTÉRÊT VÉTÉRINAIRE



LIMITES D'UTILISATION DES PHYTOCANNABINOÏDES



AUTOMÉDICATION / INTOXICATIONS

CBD AND OSTEOARTHRITIS (OA) IN DOGS

OA affects 1 in 5 adult dogs

55% of dogs with OA treated with NSAIDs experience negative side effects

CBD oil may allow you to reduce other drugs for chronic pain management

2mg of CBD oil daily can improve comfort and mobility for dogs with OA

CBD oil may prevent the progression of nerve damage from OA related joint inflammation

FAUSSES INFORMATIONS






formation ASV

Et la vente CBD au comptoir présente d'autres avantages..

DÉRIVES COMMERCIALES


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PEA: ENDOCANNABINOÏDE D'INTÉRÊT VÉTÉRINAIRE

veto zen

USAGE PEA VERSUS CBD

- Stimulation SEC
- Antiinflammatoire
- Autacoides antagonistes des lésions locales
- Pro-homéostasie
- Arthrose ?
- Troubles cognitifs ?
- Innocuité

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MERCI POUR VOTRE ATTENTION

QUESTIONS

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