**Table S1.** SANRA Score for quality assessment of the selected studies.

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **No.** | **Title** | **Justification of the article’s importance for the readership** | **Statement of concrete aims or formulation of questions** | **Description of the literature search** | **Referencing** | **Scientific reasoning** | **Appropriate presentation of data** | **Total Score** |
| **1** | PEA: A Natural Compound for Health Management. | 2 | 1 | 0 | 1 | 0 | 1 | 5 |
| **2** | The Basal Pharmacology of PEA | 1 | 2 | 1 | 0 | 1 | 0 | 5 |
| **3** | Efficacy of PEA for Pain: A Meta-Analysis | 1 | 1 | 0 | 1 | 2 | 1 | 6 |
| **4** | Synaptic Effects of PEA in Neurodegenerative Disorders | 2 | 0 | 1 | 1 | 1 | 2 | 7 |
| **5** | PEA for the treatment of pain: pharmacokinetics, safety and efficacy | 1 | 0 | 1 | 2 | 1 | 1 | 5 |
| **6** | PEA in the Treatment of Chronic Pain: A Systematic Review and Meta-Analysis of Double-Blind Randomized Controlled Trials | 1 | 2 | 0 | 2 | 1 | 0 | 6 |
| **7** | A Nutritional Approach to Keep Neuroinflammation within Physiological Boundaries-A Systematic Review | 2 | 1 | 2 | 0 | 1 | 0 | 6 |
| **8** | The Effect of PEA on Pain Intensity, Central and Peripheral Sensitization, and Pain Modulation in Healthy Volunteers-A Randomized, Double-Blinded, Placebo-Controlled Crossover Trial | 1 | 2 | 0 | 1 | 0 | 1 | 5 |
| **9** | PEA and Its Formulations on Management of Peripheral Neuropathic Pain | 0 | 2 | 1 | 0 | 0 | 2 | 5 |
| **10** | The pharmacology of PEA and first data on the therapeutic efficacy of some of its new formulations | 2 | 1 | 1 | 0 | 0 | 0 | 4 |
| **11** | Control of pain initiation by endogenous cannabinoids | 1 | 2 | 1 | 1 | 2 | 1 | 8 |
| **12** | PEA: A Natural Body-Own Anti-Inflammatory Agent, Effective and Safe against Influenza and Common Cold | 1 | 1 | 0 | 1 | 2 | 1 | 6 |
| **13** | The cellular immune response of the pea aphid to foreign intrusion and symbiotic challenge | 2 | 0 | 2 | 1 | 2 | 1 | 8 |
| **14** | A randomized controlled trial assessing the safety and efficacy of PEA for treating diabetic-related peripheral neuropathic pain. | 1 | 0 | 1 | 2 | 0 | 0 | 4 |
| **15** | PEA, a Special Food for Medical Purposes, in the Treatment of Chronic Pain: A Pooled Data Meta-analysis | 0 | 1 | 1 | 2 | 1 | 1 | 6 |
| **16** | Clinical applications of PEA in pain management: protocol for a scoping review | 2 | 1 | 2 | 2 | 1 | 2 | 10 |
| **17** | PEA Modulation of Microglia Activation: Characterization of Mechanisms of Action and Implication for Its Neuroprotective Effects | 2 | 1 | 1 | 2 | 1 | 1 | 5 |
| **18** | Glia and mast cells as targets for PEA, an anti-inflammatory and neuroprotective lipid mediator | 2 | 1 | 0 | 1 | 1 | 0 | 5 |
| **19** | Spinal nociceptive sensitization and plasma PEA levels during experimentally induced migraine attacks | 0 | 2 | 0 | 1 | 2 | 2 | 7 |
| **20** | Ultra-micronized PEA: An Efficacious Adjuvant Therapy for Parkinson's Disease | 0 | 2 | 1 | 1 | 2 | 0 | 6 |
| **21** | PEA induces microglia changes associated with increased migration and phagocytic activity: involvement of the CB2 receptor | 1 | 1 | 2 | 1 | 1 | 1 | 7 |
| **22** | PEA is a disease-modifying agent in peripheral neuropathy: pain relief and neuroprotection share a PPAR-alpha-mediated mechanism | 1 | 1 | 2 | 2 | 0 | 2 | 8 |
| **23** | Ultramicronized Palmitoylethanolamide (um-PEA): A New Possible Adjuvant Treatment in COVID-19 patients | 0 | 0 | 1 | 2 | 2 | 1 | 6 |
| **24** | PEA is a disease-modifying agent in peripheral neuropathy: pain relief and neuroprotection share a PPAR-alpha-mediated mechanism | 0 | 1 | 1 | 1 | 1 | 2 | 6 |
| **25** | Effects of PEA on Nociceptive, Musculoskeletal and Neuropathic Pain: Systematic Review and Meta-Analysis of Clinical Evidence | 2 | 1 | 0 | 0 | 2 | 1 | 6 |
| **26** | Effect of PEA on inflammatory and neuropathic pain in rats | 1 | 2 | 2 | 1 | 0 | 0 | 6 |
| **27** | PEA in the treatment of neuropathic pain: a case study | 1 | 2 | 1 | 1 | 1 | 2 | 8 |
| **28** | Effect of Ultra-Micronized Palmitoylethanolamide and Luteolin on Olfaction and Memory in Patients with Long COVID: Results of a Longitudinal Study | 2 | 2 | 2 | 0 | 2 | 0 | 8 |
| **29** | PEA, a nutraceutical, in nerve compression syndromes: efficacy and safety in sciatic pain and carpal tunnel syndrome | 0 | 2 | 1 | 0 | 0 | 0 | 3 |
| **30** | Micronized PEA reduces the symptoms of neuropathic pain in diabetic patients | 2 | 0 | 0 | 1 | 2 | 1 | 7 |
| **31** | Non-neuronal cell modulation relieves neuropathic pain: efficacy of the endogenous lipid PEA | 2 | 1 | 0 | 0 | 2 | 1 | 6 |
| **32** | Effect of Ultra-Micronized-Palmitoylethanolamide and Acetyl-l-Carnitine on Experimental Model of Inflammatory Pain | 2 | 0 | 0 | 1 | 2 | 2 | 7 |
| **33** | PEA in homeostatic and traumatic central nervous system injuries | 2 | 1 | 1 | 1 | 2 | 1 | 8 |
| **34** | PEA: problems regarding micronization, ultra-micronization and additives | 1 | 0 | 1 | 1 | 1 | 1 | 5 |
| **35** | Palmitoylethanolamide dampens neuroinflammation and anxiety-like behavior in obese mice | 2 | 1 | 1 | 2 | 1 | 1 | 8 |
| **36** | Heteroarylureas with spirocyclic diamine cores as inhibitors of fatty acid amide hydrolase | 1 | 2 | 1 | 1 | 0 | 2 | 7 |
| **37** | Therapeutic utility of PEA in the treatment of neuropathic pain associated with various pathological conditions: a case series | 1 | 2 | 1 | 2 | 0 | 2 | 8 |
| **38** | Antineuropathic profile of N-palmitoylethanolamine in a rat model of oxaliplatin-induced neurotoxicity | 1 | 1 | 2 | 1 | 0 | 0 | 5 |
| **39** | A novel composite formulation of palmitoylethanolamide and quercetin decreases inflammation and relieves pain in inflammatory and osteoarthritic pain models | 1 | 1 | 1 | 1 | 1 | 2 | 7 |
| **40** | PEA counteracts substance P-induced mast cell activation in vitro by stimulating diacylglycerol lipase activity | 0 | 0 | 1 | 1 | 1 | 2 | 5 |
| **41** | Levels of bioactive endogenous lipids and health-related quality of life in Chronic Idiopathic Axonal Polyneuropathy | 2 | 1 | 1 | 1 | 1 | 1 | 7 |
| **42** | Full inhibition of spinal FAAH leads to TRPV1-mediated analgesic effects in neuropathic rats and possible lipoxygenase-mediated remodeling of anandamide metabolism | 0 | 1 | 1 | 0 | 1 | 1 | 4 |
| **43** | Review of Alzheimer's disease drugs and their relationship with neuron-glia interaction | 2 | 2 | 2 | 1 | 1 | 2 | 10 |
| **44** | Amyotrophic lateral sclerosis treatment with ultramicronized PEA: a case report | 2 | 1 | 2 | 0 | 0 | 2 | 7 |
| **45** | Therapeutic effect of PEA in cognitive decline: A systematic review and preliminary meta-analysis of preclinical and clinical evidence | 2 | 2 | 2 | 0 | 1 | 1 | 8 |
| **46** | An Update of PEA and Luteolin Effects in Preclinical and Clinical Studies of Neuroinflammatory Events | 1 | 2 | 0 | 0 | 0 | 1 | 4 |
| **47** | Effects of Ultramicronized PEA on Mitochondrial Bioenergetics, Cerebral Metabolism, and Glutamatergic Transmission: An Integrated Approach in a Triple Transgenic Mouse Model of Alzheimer's Disease. | 1 | 2 | 0 | 1 | 2 | 1 | 7 |
| **48** | The Association of PEA with Luteolin Decreases Neuroinflammation and Stimulates Autophagy in Parkinson's Disease Model | 1 | 2 | 1 | 1 | 0 | 1 | 6 |
| **49** | Palmitoylethanolamide in CNS health and disease | 0 | 0 | 2 | 1 | 1 | 1 | 5 |
| **50** | Abnormalities in the cerebrospinal fluid levels of endocannabinoids in multiple sclerosis | 1 | 1 | 0 | 1 | 0 | 2 | 5 |
| **51** | Plasma endocannabinoid levels in multiple sclerosis | 1 | 2 | 0 | 2 | 1 | 0 | 6 |