Vascular dementia and aliamides: A new approach for the future

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Abstract

Vascular dementia (VaD) is the first usual cases of dementia after Alzheimer’s disease, causing approximately 15% of instances. Yet, unlike Alzheimer’s disease, there are no treatments to diminish the inflammatory process correlated to vascular dementia. Palmitoylethanolamide (PEA) was discovered more than five decades ago and has been proved to counteract peripheral inflammation and mast-cell degranulation, as good as to exert neuroprotective and antinociceptive effects in rats and mice experimental model. Luteolin (Lut) is an important flavone that has advantageous neuroprotective impacts both in vitro and in vivo. This mini-review gives a little outline of current information of PEA and Luteolin impact on various experimental model and the novel possible PEA-Lut use for the treatment of VaD.

Background

Vascular dementia (VaD) is a dynamic disorder that influences psychological capacities that were caused by lessened blood stream to the cerebral cortex. VaD patients may suffer both distinctive subjective impediment, for example, discouragement and tension and additionally the loss of executive capacities [1]. Until today, no other medication, excluding cholinesterase inhibitors and memantine, has demonstrated a particular advantage in the treatment of VaD, anyway they are dubious clinical criticalness; likewise Cerebrolysin has indicated advantageous impacts on VaD patients, notwithstanding, an ongoing meta-examination presumed that there is as yet lacking confirmation to prescribe it as a normal treatment for VaD [2,3]. Therefore is required to test constantly new particles, in order to find a treatment that is able to stop the progression of this pathology.

Neuroinflammation and oxidative stress (OS) has been widely correlated to be involved in the pathogenesis of both Alzheimer’s disease (AD) and VaD.

Experimental evidence suggests that after stroke, the microglia acquires a M2 phenotype, which step by step changes into a pro-inflammatory M1 phenotype in the peri-infarct area [4]. The pathologic mechanism, for example, oxidative/nitrosative stress and apoptosis can stimulate the release of a proinflammatory mediators by receptive glial cells (microglia and astrocytes), and this impact can be exacerbated by an enlargement in BBB permeability, in this manner empowering the penetration of proinflammatory factors, for example, interleukins (IL-1, IL-6) and TNF-a and prompt neurodegeneration and cell passing in various cerebral locales, including those associated with psychological capacities, for example, the hippocampus [1,5-7].

Developing confirmation exhibited that OS isn’t just connected to VaD, yet additionally to all its hazard factors, for example, diabetes, hypercholesterolemia and hyperhomocysteinemia [8-10]. The importance of OS in such a significant number of neurodegenerative issue the brain is highly susceptible to reactive oxygen species (ROS), since it is wealthy in unsaturated fats, which are sensible to peroxidation, moreover it has not a powerful antioxidant activity, and considering that it expends a ton of oxygen it is presented to a vital free-radicals amassing [11,12].

Several researches have been directed with a specific end goal to explore whether antioxidant and neuroprotective exerts a role in the prevention and treatment of VaD. In fact, in the last year, more than fifteen author all over the world, have focused their attention on the link between vascular dementia and neuroinflammation/oxidative stress relationship (Table 1).

One of the most widely studied families of molecules in recent years in the field of neuroinflammation is the family of ALIAmides.

ALIAmides stands for Autacoid Local Injury Antagonist amides (ALIAmides) and represent a group of endogenous bioactive acyl ethanolamides that include the renowned palmitoyl ethanolamide (PEA), stearoyl ethanolamide (SEA), and oleoyl ethanolamide (OEA) and that are involved in several biologic processes such as nociception, lipid metabolism and inflammations [13]. Several mechanisms describe the anti-inflammatory, anti-hyperalgesic and neuroprotective effects of PEA. In particular, PEA down-regulates mast cell activation and prevent

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their degranulation, modulates the activation of nuclear factor kB (NF-kB) and the synthesis of pro-inflammatory enzymes and promotes the activation of a cell surface cannabinoid CB2-like receptor, or a nuclear receptor of the peroxisome proliferator-activated receptors (PPARs) family [14]. However, the PEA does not have direct antioxidant action to prevent oxidative stress and counteract injury to proteins and DNA.

For this reason during the years, PEA was associated with different antioxidant molecules such as a (trans)resveratrol glucoside(s), polydatin [15-18] and (trans)polydatin [19-23] as well as a flavonoid luteolin [24-38].

Luteolin (Lut), like PEA, exerts a variety of pharmacological activities and anti-oxidant properties releated with its great ability to scavenge oxygen and nitrogen species. Luteolin has been appeared antioxidant molecules such as a (trans)resveratrol glucoside(s), polydatin [15-18] and (trans)polydatin [19-23] as well as a flavonoid luteolin [24-38].

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