Arachidonic Acid Mediators and their Role in Neurological Disease

Arachidonic acid (AA) (5, 8, 11, 14-eicosatetraenoic acid) is a polyunsaturated fatty acid, abundant in cell membrane phospholipids and mainly released upon activation of cytosolic phospholipase A2 (cPLA2). Soon after its release, AA is further metabolized by several enzymatic and non-enzymatic pathways, such as cyclooxygenase (COX) and lipoxygenase (LOX) pathways. The COX enzyme, also known as PGH-synthase (PGHS), gives rise to the production of cyclic endoperoxides (PGG2-PGH2), hence to different prostaglandins (PGs), i.e., PGD2, PGE2, PGF2α, prostacyclin (PGI2), and thromboxane (TXA2). Two isoforms of this enzyme have been identified, COX-1, the constitutive isoform, involved in various processes such as thromboxane synthesis in platelets [1, 2]; COX-2, on the other hand, is the inducible isoform involved in various processes, particularly inflammation [1, 2]. It is expressed in response to proinflammatory stimuli (different traumas, heat, cytokines, etc.), causing increased synthesis of prostanoids that contributes to the classical signs and symptoms of the inflammatory process [1]. COX-2 is predominantly found in the brain, kidney, and endothelial cells and is significantly upregulated as part of various acute and chronic inflammatory conditions.

AA mediators are involved in different neurological disorders. Prostaglandins are involved in blood-flow homeostasis and inflammation during nerve injury. Different studies show the role of AA and the increased expression of COX and PGs in nerve degeneration and regeneration after injury [2]. Moreover, prostanoid receptors can modulate Schwann cell's function in vivo and play a fundamental role in neuroinflammation [3-5].

Hence, in collaboration with “CNS & Neurological Disorders-Drug Targets,” I have prepared a thematic issue of selected papers that covers the latest knowledge on various aspects of AA's role in brain disorders. As a Guest Editor, I feel privileged to have well-known scientists who have contributed to this volume through their research papers.

Kursun et al. review the importance of AA metabolites in different neurodegenerative diseases, including Alzheimer’s Disease, Parkinson’s Disease, Amyotrophic Lateral Sclerosis, and neuropsychiatric disorders, or also in other conditions such as acute stroke, global ischemia, subarachnoid hemorrhage, and anticoagulation related haemorrhagic transformation, reporting also different treatment options.

Gorica and Calderone review the role of each AA mediator (PGD2, PGE2, PGF2α, PGI2, TXA2, LTs) in neuroinflammation and highlight the role of AA derivatives and their receptors as potential targets for innovative pharmacological therapies in central nervous system (CNS) diseases associated with neuroinflammation.

Maqoud et al. review the important role of AA and its metabolites in modulating the ATP-sensitive potassium channels (KATP). This can represent an innovative strategy for the treatment of neurodegenerative disorders.

Gwanyanya et al. have provided a review on the effects of ethanolamine in the brain as a promoter of drug movement across the blood-brain barrier. Of the ethanolamine diacyl phospholipids, those containing AA are the most abundant. The authors provide evidence that alterations of the levels of ethanolamine are associated with neurodegenerative conditions, such as Alzheimer’s disease.

Hoxha et al. review the importance of AA in multiple sclerosis (MS). The AA inflammatory mediators such as prostaglandins and leukotrienes are involved in pro-inflammatory responses in MS. The authors discuss how these mediators are altered in human and animal models. They also highlight the importance of hybrid compounds, such as COX-2 inhibitors/TP antagonists and 5-LOX inhibitors, as an innovative approach for multiple sclerosis treatment.

Altogether, the articles in this thematic issue report the fundamental role of the AA pathway and its mediators in neurological disease. They also address potential therapeutic targets on the AA pathway. It is hoped that this new information may shed light and lead to innovative drugs targeting the AA mediators and/or receptors.

CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.
ACKNOWLEDGEMENTS

Declared none.

REFERENCES


Malvina Hoxha
Department for Chemical-Toxicological and Pharmacological Evaluation of Drugs
Faculty of Pharmacy, Catholic University Our Lady of Good Counsel
Rruga Dritan Hoxha, 1000 Tirana
Albania
E-mail: m.hoxha@unizkm.al