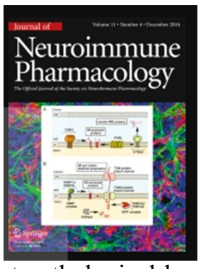
Natural immunosuppressants as a treatment for chronic insomnia targeting the inflammatory response induced by NLRP3/caspase-1/IL-1β axis activation: ~~A~~ a scooping review



https://link.springer.com/article/10.1007/s11481-023-10078-7

Abstract

Chronic insomnia is an inflammatory-related disease ~~that has an~~with an important pathological basis for ~~a variety of~~various diseases ~~and~~ which is a serious threat to ~~the a person's~~one's physical and mental health. So far, many hypotheses have been proposed to explain the pathogenesis of insomnia, ~~and in the meanwhile~~among which inflammatory mechanisms have become the focus of scientific attention. In this regard, the aim of the present scooping review is to evaluate the potential benefits of natural compounds in treatment of chronic insomnia ~~treatment~~ targeting NLRP3/caspase-1/IL-1β axis as one of the most important activators of inflammatory cascades. The data show that compounds that have the potential to cause inflammation induce sleep disorders, and that inflammatory mediators are ~~vital~~ key molecules in regulating the sleep-related activity of neurons. In the inflammatory process of insomnia, the role of NLRP3 in the pathogenesis of insomnia has been gradually considered by researchers. NLRP3 is an intracellular sensor that recognizes the widest range of pathogen-associated molecular patterns (PAMPs) and danger-associated molecular patterns (DAMPs). After identification and binding to damage factors, NLRP3 inflammasome is assembled to activate the caspase-1 and IL-1β. Increased production and secretion of IL-1β may be involved in the central nervous system dysregulation of physiological sleep. The current review reports suggest new molecular pathways involved in chronic insomnia ~~that~~ which are inhibited by application of natural compounds ~~application~~, suggesting a potential targeted therapy for managing inflammation and improving symptoms in individuals with chronic insomnia.

Introduction

Insomnia is not only a serious disease in itself but also is a risk factor for many inflammation- related diseases such as cardiovascular disease, diabetes, neurological diseases, and autoimmune diseases. Symptomatic treatment of insomnia ~~with~~ via ~~sleeping~~ sedative drugs such as benzodiazepines, z-drugs, and anticonvulsants is currently unsatisfying due to the risk of dependence and possible consequences during the day. For example, it has been reported that 15% to 40% of benzodiazepines chronic users had extreme withdrawal indications after cessation. Also, the current first-line treatment, Cognitive-Behavioral Therapy for Insomnia (CBTI), may not be available to all affected individuals because of both expense and constraints in the provider availability. ~~Therefore~~Thus, despite the high prevalence of insomnia and its complications, there is still no successful treatment for this disease, and at least half of the first-line treated people still do not experience normal sleep.

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The data ~~show~~ suggest that synthetic drugs not only ~~luck~~ lack the desired effect in improving insomnia, but also the long-term use causes significant side effects in patients. ~~Therefore~~Thus, natural compounds can be a suitable alternative to synthetic drugs. Interestingly, it has been described that some plants and their derivatives, in addition to managing neurotransmitters, have immunomodulatory properties. In this respect, some plant~~s~~-derived bioactive compounds have been introduced ~~that have~~with anti-inflammatory activity by preventing the production of pro-inflammatory cytokines such as IL-1β ~~that~~ which cause inflammation.