



Preventing and Treating Long-Haul COVID-19 and Other Types of Inflammation

All active ingredients being included are considered GRAS in the US. **Generally recognized as safe (GRAS)** is a United States Food and Drug Administration (FDA) designation that a chemical or substance added to food is considered safe by experts.

Pregnenolone

Female reproductive hormones may be protective against COVID-19:

Both allopregnanolone and its precursor pregnenolone blocked the entire TLR4 signaling pathway. Both molecules inhibited the binding of TLR4 to myeloid differentiation factor 2 (MD-2) in macrophages and the myeloid differentiation primary response 88 (MYD88) in the brain.

<https://www.news-medical.net/news/20201129/Female-reproductive-hormones-may-be-protective-against-COVID-19.aspx>

The neurosteroid pregnenolone promotes degradation of key proteins in the innate immune signaling to suppress inflammation:

Here we report that pregnenolone promotes ubiquitination and degradation of the TLR2/4 adaptor protein TIRAP and TLR2 in macrophages and microglial cells. Pregnenolone and its metabolites suppressed the secretion of tumor necrosis factor α and interleukin-6 mediated through TLR2 and TLR4 signaling. Pregnenolone has been reported to induce activation of cytoplasmic linker protein 170, and this protein has recently been shown to promote targeted degradation of TIRAP. We observed enhanced degradation of TIRAP and TLR4 suppression by cytoplasmic linker protein 170 in the presence of pregnenolone. Our experimental data reveal novel nongenomic targets of pregnenolone and provide important leads to understand its role in restoring immune homeostasis in various inflammatory conditions.

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6433066/#:~:text=Pregnenolone%20is%20capable%20of%20suppressing,to%20its%20anti%20inflammatory%20property.>

Review Article Open Access

The Role of Pregnenolone in Inflammatory Degenerative Brain Disease:

Pregnenolone-sulphate show an interesting antiinflammatory propertie, and, secreted locally into the brain by microglia cells, may play a promising role in neurodegenerative disease.

<https://www.omicsonline.org/open-access/the-role-of-pregnenolone-in-inflammatory-degenerative-brain-disease-ijm.1000121.php?aid=35410>

Neurosteroids as regulators of neuroinflammation:

Several functions of the central nervous system (CNS) are influenced by steroid hormones ([Compagnone and Mellon, 2000](#), [Mellon and Griffin, 2002](#)). Circulating steroids produced by the adrenal glands, the gonads and the placenta readily cross the blood brain barrier (BBB) and reach their target cells in the CNS by diffusion; these are termed 'neuroactive' steroids ([Mellon and Griffin, 2002](#), [Schumacher et al., 2003](#), [Starka et al., 2015](#)). In addition, the CNS has the capacity to synthesize steroids de novo ([Compagnone and Mellon, 2000](#), [Mellon and Griffin, 2002](#)). Of note, in humans, steroids, such as dehydroepiandrosterone (DHEA) and its sulfate ester (DHEAS), pregnenolone and allopregnanolone, can be found in greater amounts in the brain than in the serum ([Maggio et al., 2015](#), [Marx et al., 2006](#)). The prevailing thinking is that steroids synthesized in the CNS and circulation-derived steroids have indistinguishable effects in the CNS ([Compagnone and Mellon, 2000](#), [Mellon and Griffin, 2002](#), [Schumacher et al., 2003](#), [Starka et al., 2015](#), [Alexaki et al., 2017](#), [Charalampopoulos et al., 2006](#), [Charalampopoulos et al., 2008](#)). Therefore, in the present review, we discuss the effects of steroids on neuroinflammation independently of their origin;

<https://www.sciencedirect.com/science/article/pii/S0091302219300500>

Effect of Pregnenolone vs Placebo on Self-reported Chronic Low Back Pain Among US Military Veterans:

The use of pregnenolone in this randomized, double-blind, placebo-controlled clinical trial in 94 veterans with chronic low back pain resulted in a significant reduction in pain intensity ratings after 4 weeks of treatment.

<https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2761797>

For further details and the list of all ingredients please click on the link or visit our website www.rheumcare.com/research-ingredient-nutraceutical