Ivermectin Mechanism of Action for the treatment of COVID-19

For those wondering how an anti-parasitic medication would work effectively against a viral infection, the following explains things pretty well:

Ivermectin has been shown to inhibit the replication of severe acute respiratory syndrome coronavirus 2

(SARS-CoV-2) in cell cultures. Ivermectin acts by inhibiting the host importin alpha/beta-1 nuclear transport proteins, which are part of a key intracellular transport process that viruses hijack to enhance infection by suppressing the host antiviral response. Ivermectin is therefore a host-directed agent, which is likely the basis for its broad-spectrum activity in

vitro against the viruses that cause dengue, Zika, HIV, and yellow fever profile (NIH, 2020).

Wagstaff et al (2012) have explained that the movement of proteins between the cytoplasm and nucleus mediated by the importin superfamily of proteins is essential to many cellular processes, including differentiation and development, and is

critical to disease states such as viral disease and oncogenesis. They developed a high-throughput screen to identify specific and general inhibitors of protein nuclear import, from which Ivermectin was identified as a potential inhibitor of importin α/β-mediated transport. In their study, they characterized in detail the nuclear transport inhibitory properties of

Ivermectin, demonstrating that it is a broad-spectrum inhibitor of importin α/β nuclear import, with no effect on a range of other nuclear import pathways, including that mediated by importin β1 alone. Importantly, they established for the first time that Ivermectin has potent antiviral activity towards both HIV- 1 and dengue virus, both of which are strongly reliant on

importin α/β nuclear import, with respect to the HIV-1 integrase and NS5 (nonstructural protein 5) polymerase proteins respectively. Ivermectin would appear to be an invaluable tool for the study of protein nuclear import, as well as the basis for the development of antiviral agents.

Ivermectin has the capacity to modulate the immune

response. An uncontrolled immune response is partly responsible for the pathophysiology of COVID-19. It exerts anti-inflammatory effect by downregulating the nuclear transcription factor kappa-B and mitogen-activated protein kinase activation pathway, it may inhibit LPS-induced production of inflammatory cytokines by blocking NF-kappaB and MAP-kinase in RAW 264.7

cells (Xinxin C, 2009).

Lehrer & Rheinstein (2020) carried out a docking study to determine if Ivermectin might be able to attach to the SARS-CoV-2 spike receptor-binding domain bound with ACE2. They concluded that the Ivermectin docking that they identified may interfere with the attachment of the spike to the human cell membrane.

Other potential mechanisms of action include inhibition of the viral enzyme used to unwind its RNA, the helicase, for which it seems Ivermectin may be effective at much lower concentrations. Interaction with the Nicotinic Acetylcholine receptor that may cause immunomodulation or reduce the expression of

ACE-II, the receptor used by the virus to enter the cells (Chaccour, 2020).