

## Sea Sail Venom: a Blessing in Disguise

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### Abstract

This opinion article reports a pioneering effort in its field, indicating the potential of conotoxins as pharmacological agents for anti-adhesion adjunct therapy in the context of malaria. In a similar vein, the potential application of conotoxins as inhibitors of protein-protein interactions holds promise for the mitigation of emerging diseases such as AIDS and COVID-19.

**Keywords:** central nervous system; conotoxins; COVID-19

### Introduction

Conotoxins, also known as conopeptides, are bioactive compounds that are produced extragenomically in the venom of over 850 species of marine mollusks within the *Conus* genus [1-5]. Conotoxins have been extensively studied for many years as molecular probes and potential drug candidates for the central and peripheral nervous systems due to their strong affinity and relative specificity towards ion channels, transporter molecules, and cell receptors. In addition to their central nervous system (CNS) focus, conopeptides have the ability to influence orthosteric receptors found on the surfaces of non-excitable systems. These peptides can be utilised to investigate innovative applications that aim to inhibit abnormal cellular reactions or disrupt interactions between hosts and parasites by interacting with both endogenous and exogenous proteins.

Considering the extensive collection of conopeptides/conotoxins in the natural library, consisting of a multitude of unique compounds, it is highly probable that investigations into their functions beyond central nervous system modulation will result in significant advancements in fields that are persistently striving for more effective therapeutic strategies [5-12]. Cancer, autoimmune diseases, emerging viral diseases, fungal diseases, and malaria represent areas of investigation in which the application of venom-derived peptidic natural products can be explored.

According to recent estimates, the global incidence of malaria exceeds 500 million cases annually, with a mortality rate surpassing 400 thousand deaths [13]. *P. falciparum* malaria is widely recognised as the most severe and lethal variant of human malaria. It is noteworthy that this particular strain does not rely on the Duffy receptor for infecting red blood cells, thereby exhibiting a specific predilection for individuals of African ancestry residing in sub-Saharan Africa [14]. In the year 2017, this particular geographic area was responsible for nearly 80% of reported cases of *P. falciparum* malaria and accounted for 88% of malaria-related fatalities, with a particular emphasis on children below the age of 5 [15,

16, 17, 18, and 19]. According to the cited source, it has been observed that over 200,000 deaths occur each year as a result of low birth weight caused by placental malaria (PM). Additionally, approximately ten thousand mothers also lose their lives in relation to this condition [14]. Cerebral malaria (CM) is an additional form of malaria syndrome that is highly destructive [8-10]. It leads to severe and enduring neurological impairments, affecting nearly 100,000 children annually in Sub-Saharan Africa, where it is associated with a high mortality rate [9]. The interaction between infected erythrocytes (IE) and host receptors, known as cytoadherence, plays a crucial role in the virulence of *Plasmodium falciparum* [10-14]. Cytoadherence has been identified as a contributing factor to severe malaria, including both severe malarial anaemia (SMA) and cerebral malaria (CM). In the pursuit of novel strategies to impede the attachment of *P. falciparum*-infected erythrocytes (IE) to vascular receptors, there is potential to enhance the efficacy of existing and forthcoming chemotherapeutic interventions. This approach holds promise in addressing the formidable obstacle posed by the rapid emergence of drug resistance exhibited by *P. falciparum*. The adjunct anti-adhesion drugs under consideration do not possess direct parasitocidal properties. However, they have the potential to mitigate the development of severe malaria pathologies that are linked to the cytoadhesion of infected erythrocytes (IE). Additionally, these drugs may facilitate the clearance of IE that are obstructed by adhesion in the spleen, a phenomenon that is typically avoided due to IE cyto adhesion. Hence, it is crucial to consistently strive towards the development of novel therapeutic interventions for the treatment of *P. falciparum* malaria. This is necessary in order to stay ahead of the constantly evolving mechanisms employed by *P. falciparum* to acquire drug resistance. Furthermore, this endeavour is essential to achieve the targeted global eradication of malaria by the year 2040, as proposed by previous research.

### A cure

According to a recent study [2], there is evidence to suggest that sea snail venom may offer novel therapeutic options for the treatment of Malaria. The venomous strand of armoured marine gastropods possesses distinctive compounds that exhibit potential for potent medicinal properties. The compound exhibits a wide range of potential applications, encompassing areas such as cancer therapeutics and analgesics.

Annually, the global incidence of malaria surpasses 500 million cases, resulting in a mortality rate exceeding 400,000 individuals. Severe manifestations of malaria, such as Plasmodium Falciparum infection, have the potential to result in fatality despite the administration of existing antimalarial medications. Furthermore, the effectiveness of malaria vaccines has been found to be restricted. Currently, it is postulated by researchers that the utilisation of anti-adhesion drugs could potentially serve as a pivotal factor in substantially enhancing rates of survival.

Anti-adhesion drugs do not possess the ability to eliminate the infectious agent. In contrast, their function lies in the prevention of harm to the host organism by impeding the attachment to and invasion of host cells and tissues. The study conducted by researchers showcased the capacity of snail venoms to disrupt protein-protein and protein-polysaccharide interactions. Contoxins have the potential to serve as inhibitors of protein-protein interactions, thereby offering therapeutic benefits in the treatment of diseases such as AIDS and COVID-19.

The utilisation of venom peptides derived from cone snails exhibits promising potential in the treatment of numerous diseases through the application of blockage therapies. The potential therapeutic application of contoxins derived from the venom of Conus nux, a marine gastropod species, in the treatment of malaria has been demonstrated by researchers. Contoxins refer to a collection of neurotoxic peptides that have been extracted from the venom of the cone snail found in marine environments. This study offers significant insights that contribute to the advancement of novel and economically efficient therapeutic approaches. Contoxins have been extensively investigated for several decades as molecular probes and potential therapeutic agents that specifically target the central

nervous system. Snails incapacitate their prey through targeted modulation of its central nervous system.

### Concluding Remark

Although the observed outcomes have thus far been limited to laboratory settings, the researchers assert that this finding has the potential to facilitate the development of future pharmaceutical interventions for the treatment of severe malaria cases. Furthermore, it may also hold promise for addressing other diseases that rely on analogous protein-based interactions, such as cancer, AIDS, and COVID-19. It is asserted that the discoveries presented in this study broaden the pharmacological scope of conotoxins/conopeptides, as they demonstrate their capacity to interfere with protein-protein and protein-polysaccharide interactions that play a direct role in the development of the disease. This discovery offers novel opportunities for investigating the application of venom peptides in the prospective management of numerous diseases that can be ameliorated through the use of blockage therapies.

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