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FACULDADE DE MEDICINA

Davi Gomes Angstmam

Isolamento e Caracterização de um composto antinociceptivo do veneno de *Crotalus durissus terrificus*

Dissertação apresentada ao Programa de Doenças Tropicais da Faculdade de Medicina, Universidade Estadual Paulista "Júlio de Mesquita Filho", Câmpus de Botucatu, como parte dos requisitos para a obtenção do título de mestre.

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ATA DA DEFESA PÚBLICA DA DISSERTAÇÃO DE MESTRADO DE DAVI GOMES ANGSTMAM, DISCENTE DO PROGRAMA DE PÓS-GRADUAÇÃO EM DOENÇAS TROPICAIS, DA FACULDADE DE MEDICINA - CÂMPUS DE BOTUCATU.

Aos 30 dias do mês de maio do ano de 2025, às 9h, no(a) Auditório do Centro de Estudos de Venenos e Animais Peçonhentos (CEVAP), realizou-se a defesa de DISSERTAÇÃO DE MESTRADO de DAVI GOMES ANGSTMAM, intitulada **Isolamento e caracterização de um composto antinociceptivo do veneno de Crotalus durissus terrificus**. A Comissão Examinadora foi constituída pelos seguintes membros: Prof. Dr. RUI SEABRA FERREIRA JUNIOR (Orientador(a) - Participação Presencial) do(a) Centro de Estudos de Venenos e Animais Peçonhentos - Unesp, Dra. BRUNA CAVECCI MENDONÇA (Participação Presencial) do(a) Centro de Estudos de Venenos e Animais Peçonhentos - Unesp, Prof. Dr. PATRICK JACK SPENCER (Participação Virtual) do(a) Comissão Nacional de Energia Nuclear / Instituto de Pesquisas Energéticas e Nucleares- IPEN. Após a exposição pelo mestrando e arguição pelos membros da Comissão Examinadora que participaram do ato, de forma presencial e/ou virtual, o discente recebeu o conceito final: aprovado. Nada mais havendo, foi lavrada a presente ata, que após lida e aprovada, foi assinada pelo(a) Presidente(a) da Comissão Examinadora.

Prof. Dr. RUI SEABRA FERREIRA JUNIOR

Resumo

A dor é uma sensação relacionada a um atual ou potencial dano tecidual, podendo estar associada ao sintoma de uma doença ou definida como a própria doença, no caso de dor crônica. O tratamento mais recomendado para o alívio da dor, principalmente a dor física, são os analgésicos. No entanto, o uso destes fármacos apresenta efeitos adversos como tolerância e dependência quando utilizados de maneira contínua. Uma das alternativas para o desenvolvimento de novos medicamentos é o investimento em estudos de venômica. O presente trabalho teve como objetivo isolar e caracterizar uma molécula de baixa massa molecular presente no veneno de *Crotalus durissus terrificus* (*C.d.t.*) e avaliar seu potencial efeito antinociceptivo. Para tanto foram utilizados métodos de purificação e isolamento por HPLC-RP seguidos de testes biológicos como o teste da formalina, retirada de cauda e *rota-rod*, a fim de identificar a molécula com a respectiva propriedade. Os métodos utilizados para separar os componentes de baixa massa foram eficazes e foi possível identificar um composto no veneno de *C.d.t* de massa molecular aproximada de 412 Da, que apresentou atividade anti-inflamatória e analgésica por via oral e intraperitoneal. Ensaios futuros deverão ser realizados para a sua identificação e mecanismo de ação, bem como avaliação de possíveis efeitos tóxicos e colaterais.

Abstract

Pain is a sensation related to current or potential tissue damage and may be associated with the symptom of a disease or defined as the disease itself, in the case of chronic pain. The most recommended treatment of pain, especially physical pain, is analgesics. However, the use of these medications presents adverse effects such as tolerance and dependence when used continuously. One of the alternatives for the development of new drugs is to invest in studies of the toxinology of animal venoms. The present study aimed to isolate and characterize a low molecular weight molecule present in the venom of *Crotalus durissus terrificus* (C.d.t.) and to evaluate its potential antinociceptive effect. For this purpose, purification and isolation methods by HPLC-RP were used, followed by biological tests such as the formalin test, tail flick and rota-rod, in order to find a molecule with the respective property. The methods used to separate the low-mass components were effective and it was possible to identify a compound in the C.d.t venom with an approximate molecular mass of 412 Da, which presented anti-inflammatory and analgesic activity by oral and intraperitoneal routes. Future tests should be performed to identify its mechanism of action, as well as to evaluate possible toxic and side effects.

Sumário

CAPÍTULO – I: Exploring the Pain-Relieving Potential: Unveiling Analgesic Properties in Venoms and Toxins

6. Conclusão

Com base nos resultados obtidos, o presente estudo sugere a presença de pelo menos um novo composto presente no veneno da serpente *Crotalus durissus terrificus* com efeito antinociceptivo em modelos *in vivo* diferente do que já foi estudado, sendo um possível candidato a tornar-se um fármaco. No entanto, ainda restam experimentos exploratórios a serem realizados para constatar a real eficácia da molécula, se esta é ausente de efeitos tóxicos e qual o seu real mecanismo de ação.

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Anexo 1