

Disruption of membrane integrity by the bacteria-derived antifungal jagaricin.

Fischer D, Gessner G, Fill TP, Barnett R, Tron K, Dornblut K, Kloss F, Stallforth P, Hube B, Heinemann SH, Hertweck C, Scherlach K, Brunke S (2019) Disruption of membrane integrity by the bacteria-derived antifungal jagaricin. *Antimicrob Agents Chemother* 63(9), e00707-19.

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Abstract

Jagaricin is a lipopeptide produced by the bacterial mushroom pathogen *Janthinobacterium agaricidamnosum*, the causative agent of mushroom soft rot disease. Apart from causing lesions in mushrooms, jagaricin is a potent antifungal active against human-pathogenic fungi. We show that jagaricin acts by impairing membrane integrity, resulting in a rapid flux of ions, including Ca^{2+} , into susceptible target cells. Accordingly, the calcineurin pathway is required for jagaricin tolerance in the fungal pathogen *Candida albicans*. Transcriptional profiling of pathogenic yeasts further revealed that jagaricin triggers cell wall strengthening, general shutdown of membrane potential-driven transport, and upregulation of lipid transporters - linking cell envelope integrity to jagaricin action and resistance. Whereas jagaricin shows haemolytic effects, it exhibited either no or low plant toxicity at concentrations at which the growth of prevalent phytopathogenic fungi is inhibited.

Therefore, jagaricin may have potential for agricultural applications. The action of jagaricin as a membrane-disrupting antifungal is promising, but would require modifications for use in humans.

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