Title:	Curcumin Inhibits Membrane-Damaging Pore-Forming Function of the β-Barrel Pore-Forming Toxin Vibrio cholerae Cytolysin
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Abstract:	Vibrio cholerae cytolysin (VCC) is a β-barrel pore-forming toxin (β-PFT). Upon encountering the target cells, VCC forms heptameric β-barrel pores and permeabilizes the cell membranes. Structure-function mechanisms of VCC have been extensively studied in the past. However, the existence of any natural inhibitor for VCC has not been reported yet. In the present study, we show that curcumin can compromise the membrane-damaging activity of VCC. Curcumin is known to modulate a wide variety of biological processes and functions. However, the application of curcumin in the physiological scenario often gets limited due to its extremely poor solubility in the aqueous environment. Interestingly, we find that VCC can associate with the insoluble fraction of curcumin in the aqueous medium and thus gets separated from the solution phase. This, in turn, reduces the availability of VCC to attack the target membranes and thus blocks the membrane-damaging action of the toxin. We also observe that the soluble aqueous extract of curcumin, generated by the heat treatment, compromises the pore-forming activity of VCC. Interestingly, in the presence of such soluble extract of curcumin, VCC binds to the target membranes and forms the oligomeric assembly. However, such oligomers appear to be non-functional, devoid of the pore-forming activity. The ability of curcumin to bind to VCC and neutralize its membrane-damaging activity suggests that curcumin has the potential to act as an inhibitor of this potent bacterial β-PFT.
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