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Bee Venom Proteins Modulate the Ability of Phospholipid Membranes of the Myelin Sheath and Endoplasmic Reticulum to Absorb Protons from Bulk Water: Pharmacological Relevance

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INTRODUCTION & AIM

Experimental evidence has shown that the rate of ATP synthesis correlates more strongly with proton movement along the surface of the inner mitochondrial membrane (IMM) than with the transmembrane proton concentration gradient in the bulk aqueous phase. This has prompted a revision of the classical chemiosmotic theory of mitochondrial ATP production. It has been proposed that lateral proton transport along the IMM surface generates an electric potential that drives ATP synthase activity. Moreover, recent studies have reported proton accumulation and storage on the membranes of the myelin sheath and endoplasmic reticulum (ER), suggesting that surface-based energy storage via absorbed protons may be a fundamental principle of cellular bioenergetics. In this study, we examined whether membranes composed of different types of phospholipids and those enriched with acidic bee venom proteins differ in their capacity to enhance proton absorption at the membrane surface.

METHOD

Five types of phospholipids commonly found in myelin sheath and ER membranes were purified using immunoaffinity chromatography. Anionic and basic protein isoforms were isolated from bee venom via CM Sephadex C-50 chromatography. Liposomal membranes were prepared through ultrasonic frequency dispersion of phospholipid suspensions. Proton absorption at the membrane surface was assessed by measuring pH differences between liposome suspensions and pure water.

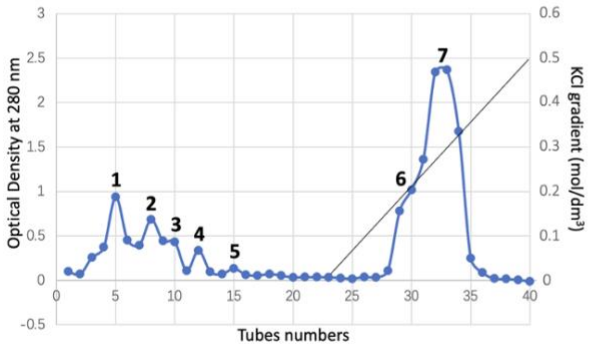

Figure 1. The cation exchange chromatography of 1.0 g of crude bee venom on a CM Sephadex C-50 column (1.5 × 35 cm). The elution profile, measured by absorbance at 280 nm, reveals seven pooled fractions. The venom was initially eluted with a 10 mM Tris buffer (pH 8.5), followed by a linear salt gradient using the same buffer containing 0.5 M KCl, starting at tube 23.

RESULTS & DISCUSSION

Membranes of liposomes enriched with anionic proteins showed enhanced proton absorption compared to protein-free liposomal membranes. Among all protein-free liposomal membrane, phosphatidylethanolamine membrane showed the highest proton absorption. Among all liposomal membranes enriched with acidic proteins, phosphatidylserine membrane exhibited the highest proton absorption.

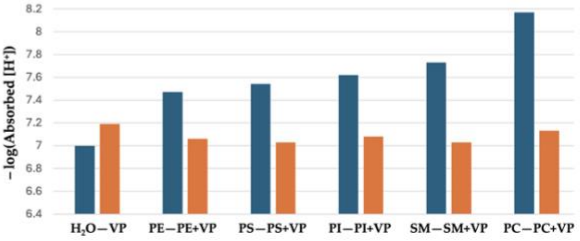

Figure 4. Absorption of hydrogen ions by acidic proteins (AP) and various liposome membranes. The negative logarithm of absorbed [H^+] is shown for AP in water and for membranes of liposomes composed of different phospholipids, both with and without VP. Emerald bars represent control samples (ddH_2O and pure phospholipid liposomes). Orange bars represent AP in ddH_2O and liposome membranes that incorporate VP. Phospholipid abbreviations: PE, phosphatidylethanolamine; PS, phosphatidylserine; PI, phosphatidylinositol; SM, sphingomyelin; PC, phosphatidylcholine.

This line of inquiry possesses considerable pharmacological relevance due to its elucidation of novel mechanisms governing cellular bioenergetics and energy storage. Such insights are foundational for devising targeted pharmaceutical strategies to ameliorate the cellular energy deficits characteristic of various pathologies and degenerative aging processes.

CONCLUSION

This research holds considerable pharmacological relevance by elucidating novel bioenergetic mechanisms that regulate cellular energy accumulation and storage. A deeper comprehension of these processes may facilitate the development of targeted pharmaceuticals designed to offset the cellular energy decline observed in pathological states and degenerative aging.

FUTURE WORK / REFERENCES

Morelli, A.M.; Saada, A.; Scholkmann, F. Myelin: A possible proton capacitor for energy storage during sleep and energy supply during wakefulness. *Prog Biophys Mol Biol* **2025**, 196, 91-101.