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## Bicarbonate Alters Bacterial Susceptibility to Antibiotics by Targeting the Proton Motive Force

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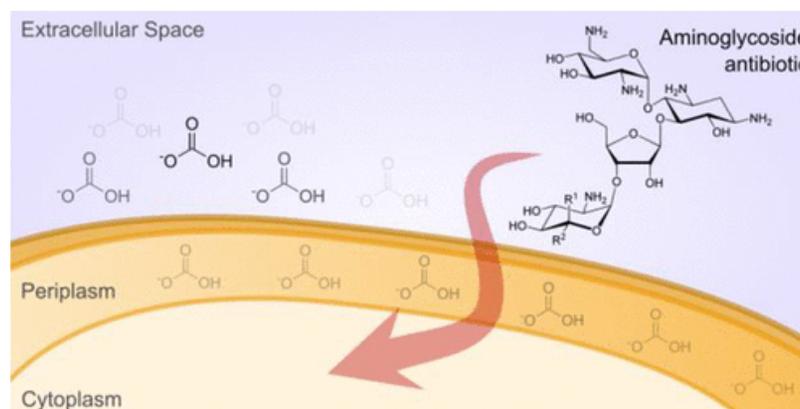
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## Abstract



The antibacterial properties of sodium bicarbonate have been known for years, yet the molecular understanding of its mechanism of action is still lacking. Utilizing chemical–chemical combinations, we first explored the effect of bicarbonate on the activity of conventional antibiotics to infer on the mechanism. Remarkably, the activity of 8 classes of antibiotics differed in the presence of this ubiquitous buffer. These interactions and a study of mechanism of action revealed that, at

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Several components of innate immunity were enhanced by a physiological concentration of bicarbonate. Our findings implicate bicarbonate as an overlooked potentiator of host immunity in the defense against pathogens. Overall, the unique mechanism of action of bicarbonate has far-reaching and predictable effects on the activity of innate immune components and antibiotics. We conclude that bicarbonate has remarkable power as an antibiotic adjuvant and suggest that there is great potential to exploit this activity in the discovery and development of new antibacterial drugs by leveraging testing paradigms that better reflect the physiological concentration of bicarbonate.

**KEYWORDS:** bicarbonate buffer system, antibiotic activity, drug discovery ▾

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- Figures S1–S7, checkerboard analyses for different antibiotics and clinical isolates and mechanistic studies; Table S1, MIC data for antibiotics in the presence of bicarbonate; Table S2, physiochemical properties of fluoroquinolones; Table S3, chemical genomic interactions; Table S4, MIC data against pathogens; Table S5, MIC data for components of innate immunity ([PDF](#))

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