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Suppressive drug combinations and their potential to combat antibiotic resistance.

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Abstract

Antibiotic effectiveness often changes when two or more such drugs are administered simultaneously and unearthing antibiotic combinations with enhanced efficacy (synergy) has been a longstanding clinical goal. However, antibiotic resistance, which undermines individual drugs, threatens such combined treatments. Remarkably, it has emerged that antibiotic combinations whose combined effect is lower than that of at least one of the individual drugs can slow or even reverse the evolution of resistance. We synthesize and review studies of such so-called 'suppressive interactions' in the literature. We examine why these interactions have been largely disregarded in the past, the strategies used to identify them, their mechanistic basis, demonstrations of their potential to reverse the evolution of resistance and arguments for and against using them in clinical treatment. We suggest future directions for research on these interactions, aiming to expand the basic body of knowledge on suppression and to determine the applicability of suppressive interactions in the clinic.

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