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Summary

IDENTIFICATION AND PRECLINICAL EVALUATION OF 2-METHOXY-1,4-NAPHTHOQUINONE AS A NOVEL NON-ANTIBIOTIC AGENT FOR ERADICATING HELICOBACTER PYLORI: FROM HIGH-THROUGHPUT SCREENING TO IN VIVO VALIDATION

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Gut Microbiota | Stomach & H. Pylori | Mechanisms & Personalised Medicine | Digestive Oncology | Oesophagus

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2-methoxy-1,4-naphthoquinone (MNQ), identified through high-throughput screening of 1,905 traditional Chinese medicine monomers, demonstrated potent bactericidal activity against multidrug-resistant H. pylori with eradication efficacy comparable to or exceeding standard quadruple therapy in a mouse infection model.

KEY POINTS

- MNQ exhibited broad-spectrum bactericidal activity against multiple multidrug-resistant H. pylori clinical isolates, including a levofloxacin- and metronidazole-resistant strain, with no detectable cytotoxicity in gastric epithelial cells.
- In vivo, MNQ significantly reduced bacterial load and gastric inflammation in a murine infection model, achieving eradication efficacy comparable to or exceeding standard quadruple therapy.
- Mechanistic analyses identified respiratory chain complex I as the primary target, with LiP-MS supporting direct engagement of the NADH-ubiquinone oxidoreductase subunit NQO5, leading to increased superoxide production, ATP depletion, and lethal oxidative stress.
- 16S rRNA sequencing demonstrated that MNQ had minimal impact on gut microbiota composition and diversity, unlike antibiotic treatment.
- No observable pathological damage was detected in kidney, liver, spleen, lung, or heart at therapeutic doses in the mouse model.

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