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Resveratrol and Red Wine Extracts Inhibit the Growth of *CagA+* Strains of *Helicobacter pylori* *In Vitro*

Gail B. Mahady, Ph.D, Susan L. Pendland, Pharm.D, and Lucas R. Chadwick, Ph.D

Department of Pharmacy Practice UIC/NIH Center for Botanical Dietary Supplements Research
College of Pharmacy, University of Illinois at Chicago Chicago, Illinois

TO THE EDITOR: In 1994, *Helicobacter pylori* was classified as a group I carcinogen and a definite cause of gastric cancer in humans by the International Agency for Research on Cancer (1). Since then, *H. pylori* has been epidemiologically linked to adenocarcinoma of the distal stomach (2,3), and a recent study has also found a positive association between *H. pylori* infection and colorectal adenomas (4). *CagA* is the strain-specific *H. pylori* gene that has been linked to the development of premalignant and malignant histological lesions (5). Thus, susceptibility of *cagA+* *H. pylori* strains is of note because, as compared with *cagA-* strains, infections caused by *cagA+* strains significantly increase the risk for developing severe gastric inflammation, atrophic gastritis, and noncardia gastric adenocarcinoma (5). Previously, we have demonstrated that resveratrol, a stilbene from red wine, inhibited the growth of 15 clinical strains of *H. pylori* *in vitro* and suggested that the anti-*H. pylori* activity of resveratrol may play a role in its chemopreventative effects (6). In this investigation, the antibacterial activities of two red wine extracts (Pinot Noir) and resveratrol were assessed against five *cagA+* *H. pylori* strains: accession numbers M23-3, GTD7-13, G1-1, SS1 (Sydney Strain *cagA+*), and the ATCC 43504 (Rockville, MD) possessing the *cagA+* gene and expressing vacuolating cytotoxin. The *H. pylori* *cagA+* strains were obtained from Drs. Richard Peek and Dawn Israel, Department of Pathology, Vanderbilt University School of Medicine, Nashville, TN. Susceptibility testing was performed with the agar dilution procedure, and all other methods were as previously described (6). Red wine extracts (Pinot Noir) were prepared, one by concentrating and drying under reduced pressure, and the second by separating the alcohol-soluble and -insoluble components. The second extract was prepared by dissolving 1500 ml of red wine in 3 L of methanol, concentrating under reduced pressure, filtering, and collecting both the filtrate (alcohol soluble) and the particulate matter (alcohol insoluble). The filtrate was termed a *methanol-soluble extract*, and the particulate matter was termed a *methanol-insoluble extract*. The methanol-soluble extract was not active in our assay at concentrations up to 500 $\mu\text{g/ml}$. However, both the methanol-insoluble and the concentrated red wine extracts were active against all *cagA+* HP strains, with minimum inhibitory concentrations (MIC) of 25 $\mu\text{g/ml}$ and 50 $\mu\text{g/ml}$, respectively (range of 25–50 $\mu\text{g/ml}$). Resveratrol was also active against all five strains, with an MIC of 12.5 $\mu\text{g/ml}$ (range of 6.25–25 $\mu\text{g/ml}$). The control drug, amoxicillin, had an MIC range of 0.0039 to 0.25 $\mu\text{g/ml}$. These data demonstrate that both red wine and resveratrol inhibit the growth of *H. pylori* *cagA+* strains *in vitro* and further support their role as chemopreventive agents.

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