

In vitro* effect of bergamot (*Citrus bergamia*) juice against *cagA*-positive and-negative clinical isolates of *Helicobacter pylori

N. Ferlazzo¹, A. Filocamo¹, C. Bisignano², S. Cirimi¹, G. Mandalari¹, M. Navarra¹

¹Dept of Drug Sciences and Products for Health, University of Messina, Messina, Italy

²Dept of Biological and Environmental Sciences, University of Messina, Italy

Helicobacter pylori infection has been associated with chronic gastritis, peptic ulcer and gastric carcinoma as over half of the world's population is colonized with this gram-negative bacterium. Because to the increasing antibiotic resistance, its eradication rates fails in a great portion of patients. A number of studies show that molecules largely distributed in commonly consumed fruits and vegetables may have antimicrobial activity. *Citrus bergamia* Risso et Poiteau (bergamot) is an endemic plant of the Calabrian region in Southern Italy mostly used for the extraction of its essential oil from the fruit peel, while bergamot juice (BJ), obtained from the endocarp of the fruit, is considered a byproduct barely utilized by the food industry.

The aim of the present study was to investigate the effect of BJ against *Helicobacter pylori in vitro*. The potential therapeutic combination between BJ and the antibiotics amoxicillin (AMX), clarithromycin (CLA) and metronidazole (MTZ) has also been evaluated.

The minimum inhibitory concentration (MIC) of BJ, AMX, CLA and MTZ against 2 ATCC and 32 clinical isolates of *H. pylori* was assayed according to Clinical and Laboratory Standards Institute. The checkerboard method was used to determine the efficacy of the association BJ with the three reference antibiotics. Killing curves were performed on the two *cagA*-positive ATCC strains of *H. pylori* (ATCC 43504 and ATCC 49503), on the clinical isolate *cagA*-positive HP6 strain of *H. pylori* and on the clinical isolate *cagA*-negative HP61 strain of *H. pylori*.

BJ (2.5%, v/v) inhibited the growth of 50% of the *H. pylori* clinical isolates, whereas 5% (v/v) inhibited 90%. AMX was the most effective antibiotic against the reference strains and the clinical isolates, followed by CLA and MTZ. In the combination assays, synergism was observed between BJ and AMX and between BJ and MTZ against both the reference strains and the clinical isolates. Indifference was observed between BJ and CLA.

In conclusion, BJ was effective *in vitro* against *H. pylori* and the genotype status of the clinical strains may have an impact on its susceptibility. The synergistic combination of BJ and antibiotics could be used as novel strategy to prevent or treat resistance.

This research was supported by a grant from Calabria Region (PSR Calabria 2007/2013 misura 124, project 'ABSIB').