Antibacterial and Anti-Adherent Properties of a Grape Seed Extract against *Helicobacter pylori*

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Background: *Helicobacter pylori* (*H. pylori*) is one of the most common human bacteria infecting more than 50% of the world's population. It is the most common etiologic agent of infection-related cancers, which accounts for around 6% of the global cancer burden. Conventional antibiotic therapies are inefficient in 20% of cases, and the efficacy of eradication treatments has been extremely compromised primarily because of the increased resistance to antibiotic agents. Therefore, the search for natural and sustainable alternatives to the use of antibiotics is a serious challenge.

Objective: The present study was aimed to evaluate the antibacterial and anti-adherent activities of a grape seed extract against *H. pylori*.

Methods: GSE was fractionated according to molecular mass (F1, >10 kDa and F2, <10 kDa). Seven resistant antibiotic strains of *H. pylori* were used (Hp44, Hp48, Hp53, Hp58, Hp59, and Hp61). For antibacterial activity, the *H. pylori* strains were incubated with GSE and its fractions (2 mg/mL) for 48h at 37ºC and colony forming units (CFU/mL) were determined. For anti-adherent activity, human gastric AGS cells were infected with *H. pylori* strains for 2h. After washing, AGS cells and adherent bacteria were treated with GSE and fractions (2 mg/mL) for 2h and CFU were determined.

Results: GSE significantly ($p<0.05$) inhibited the growth of all tested *H. pylori* strains after 48 h of treatment. Reduction of log CFU/mL was from 2.87 to 5.79 depending of the *H. pylori* strain. Although both fractions contributed to the antibacterial activity, F1 showed highest antibacterial activity. It shown a log reduction of CFU/mL ranging from 2.19 to 4.89. Antibacterial activity of F2 resulted between 1.24 and 3.20 log CFU/mL. All *H. pylori* strains showed adhesion capacity to gastric AGS cells. Adherence was higher for Hp53, Hp58, Hp59, and Hp61 strains than for Hp44 and Hp48 strains. However, adherence of all *H. pylori* strains was significantly ($p<0.05$) reduced by GSE. Both fractions contributed in a similar way to the reduction of adhesion as compared with the positive control.

Conclusions: These results suggest that GSE and fractions used in the present study may prevent the colonization of gastric cells by *H. pylori*. Therefore, GSE could be a natural and sustainable tool to treat *H. pylori* infection, providing an alternative for the 20% of infected people with symptoms for whom antibiotic treatments are not effective. In addition, the recycling of wine industry by-products could contribute to their revalorization, reducing the environmental footprint.