Summary

Even though the prevalence of *Helicobacter pylori* infections is on the decline, global infection rates remain high, emphasising the need for alternative treatment strategies. Existing therapeutic regimens often fail due to the increasing rates of antibiotic resistance and medication non-adherence of patients.

Several natural compounds, especially polysaccharides, have exhibited *in vitro* anti-adhesive activity against *H. pylori* and thus target the first step in the development of *H. pylori's* pathogenicity. Highly-esterified type I rhamnogalacturonans (ORG-I-Ac) have been characterised as the main compounds of an aqueous, dialysed extract from immature okra fruits, *Abelmoschus esculentus*, and have shown to strongly inhibit the adhesion of *H. pylori* J99 to AGS cells (IC_{50} = 550.8 ± 1.13 µg/mL). In general, adhesion of *H. pylori* is mainly mediated by outer membrane proteins (adhesins) and lipopolysaccharides (LPS). The development and validation of a specific ELISA, using recombinantly expressed blood group antigen binding adhesin (BabA) and its natural ligand Lewis^b (Le^b), indicated a strong interaction between ORG-I-Ac and BabA (IC_{50} = 17.6 ± 1.05 µg/mL). This interaction was verified using isothermal titration calorimetry. Moreover, a solid-phase binding assay with recombinant Galectin-3, the gastric epithelial cell receptor for the LPS O-antigen of *H. pylori*, indicated that LPS – Galectin-3 adhesion is also significantly inhibited by ORG-I-Ac (222.2 ± 1.76 µg/mL).

To better understand the anti-adhesive properties of rhamnogalacturonans, the following studies included pectins from different sources (apple, citrus, and sugar beet). Structural analyses of these pectins were performed to determine their respective monosaccharide composition, linkage analysis, stereochemistry, molecular weight, uronic acid content, degree of esterification, and viscosity. These data revealed the predominant presence of homogalacturonans (HG) and minimal amounts of rhamnogalacturonan I (RG-I) units, mainly substituted with galactose side chains. Depending on the pectin's source, additional neutral sugar side chains, with arabinose, glucose, and xylose residues, were identified.

Although all pectins had structural similarities to ORG-I-Ac, only apple pectin (Co. Roth) and sugar beet pectin (Co. Suedzucker) had significant anti-adhesive effects against *H. pylori* J99 (17 ± 9 % and 13 ± 11 % inhibition, respectively, at 1 mg/mL). Interestingly, all pectins tested influenced the adhesion of the clinical isolate *H. pylori* strain 25140; however the effect was lower (12 - 34 % inhibition; 1 mg/mL) compared with ORG-I-Ac (53 ± 12 % inhibition; 1 mg/mL). In general, anti-adhesive effects were only observed with the pre-treatment of the bacteria, indicating that the pectins interfere with the bacterial surface.

Similar to ORG-I-Ac, apple pectin (Co. Roth) blocked the BabA – Le^b interaction in a concentration-dependent manner (73 ± 8 % inhibition; 1 mg/mL) as well as the LPS – Galectin-3 interaction (82 ± 3 % inhibition; 1 mg/mL).

Furthermore, a sensitive microviscosimetric method was used to study the interaction between the anti-adhesive polysaccharides and mucin. ORG-I-Ac and apple pectin (Co. Roth) showed mucoadhesive properties. From this it can be deduced that these polysaccharides can accumulate in or on the gastric mucus layer.

Considering these mucoadhesive effects and the anti-adhesive properties of apple pectin (Co. Roth), a smart and specific drug delivery system, targeting *H. pylori*, was developed and successfully initiated. For this purpose, liposomes were coated with apple pectin and encapsulated with amoxicillin (encapsulation efficiency: 83 ± 3 %). As expected, the coated liposomes interacted with the mucus, improving the contact of the formulation with the bacterium. Fluorescence microscopic investigations (wide-field optical microscopy and confocal laser scanning microscopy) supported this direct interaction. Furthermore, the liposomes showed an initial burst release of the antibiotic cargo, which was associated with cytotoxic effects against *H. pylori*. This smart drug delivery system enabled the release of antibiotic into the direct vicinity of *H. pylori* and thus may increase medication adherence of patients, as their antibiotic dose size along with concomitant adverse drug reactions may be reduced.