Summary

Helicobacter pylori is a highly specialized gram negative bacterium which colonizes the human stomach. The specific adhesion to the gastric mucosa is an essential first step for the development of its pathogenicity. Therefore the prevention of bacterial adhesion by natural compounds as a new cytoprotective strategy against *H. pylori* and the mechanistic background of such interactions exhibited the focus of this thesis. For that purpose two new *in vitro* methods were developed and validated, aiming on one hand the quantification of the antiadhesive effects of test compounds against *H. pylori* adhesion to gastric epithelial cells and on the other hand to clarify the specificity of compound interactions with the respective bacterial adhesins.

By a bioassay-guided fractionation from a tryptic digest of *Pisum sativum* L. protein two highly antiadhesive active fractions were identified (F3 and F3.3), inhibiting at 0.5 mg/mL *H. pylori* adhesion *in vitro* to human gastric AGS cells and *in situ* to gastric tissue sections by up to 80%. Within complex fractions the sequences of an undeca- and a tridecapeptide (S3 and S5) were identified by mass spectrometry as major inhibitors of bacterial adhesion and were further shown to interact specifically with the *H. pylori* adhesin BabA. This novel interaction mode of BabA with peptide motifs was studied within structure-activity investigations also with synthetic derivatives of S3. Experiments identified the tripeptide Asp-Ala-Phe as an important motif for the activity of S3. Still, the activity of S3 was not excelled by the derivatives, suggesting that the entire eleven amino acid long sequence is necessary for its antiadhesive activity. Moreover, complex peptide fractions (F3 and F3.3) had higher inhibiting effects than the purified undecapeptide, being due to a consequence of simultaneous interactions with four bacterial outer membrane proteins (OMPs), namely BabA, SabA, HpaA and a fibroncetin binding adhesin. Antiadhesive pea peptides therefore exhibit potent promising alternatives for prophylaxis and prevention of reinfections after antibiotic regimes against *H. pylori* infections.

Also *N*-phenylpropenoyl-L-amino acid amides (NPAs) as typical compounds from *Theobroma cacao* L. seeds, were identified with up to 30% inhibition *in vitro* as moderate adhesion blockers against *H. pylori* with specific inhibition of BabA. For structure-activity relationship 24 homologous NPAs (2 mM) were investigated on potential antiadhesive effects against *H. pylori* adhesion to AGS cells. Dihydroxylation of the aromatic molecule part was shown to be necessary for activity; methoxylation decreased activity; high polarity of the amino acid is a prerequisite for activity.

During these investigations of NPAs, interaction of L-dopa with *H. pylori* OMPs got obvious. This was congruent with reports published in literature on differing L-dopa plasma levels after p.o. application of this drug in *H. pylori* positive Parkinson's disease patients. During detailed *in vitro* studies significant time- and concentration-dependent adsorption on bacterial OMPs was firstly demonstrated, leading to diminished concentrations of L-dopa for synthetic bioavailability. In correlation bacterial adhesion was also clearly reduced at 5.1 mM L-dopa *in vitro* and *in situ* by up to 22% and 40% respectively. Changes in dosage regimes, for *H. pylori* positive patients with Parkinson's disease, need to be considered.

Beside adhesion blockers, interacting specifically with distinct single adhesins and leading to about 20 to 30% inhibition rates, total adhesion blockers were identified within a glycoprotein/polysaccharide mixture from immature fruits of *Abelmoschus esculentus* L. (Okra). This complex mixture interacted as multi-targeted inhibitors against BabA, SabA, HpaA and an unknown fibronectin-binding adhesin.

Within Real-Time PCR gene expression studies it was shown that the identified adhesion blockers, with exception of those isolated from okra fruits, do not exhibit significantly influence the expression of adhesins (babA, alpA, alpB, hpaA, hopZ and oipA) and other virulence factors (cagA, cagL, cagα, vacA, ureA and ureI). An aqueous extract of immature okra fruits downregulated in an unknwon mechanism the expression of babA, alpA and alpB. Therewith antiadhesive compounds do not enhance and may even decrease *H. pylori* virulence. Furthermore, these results strongly suggest that regulation of *H. pylori* adhesins is not directly associated with the expression of the various virulence factors.