Summary

I) The antiadhesive potential of a quantified aqueous extract from the leaves of *Orthosiphon stamineus* Benth. (OWE) as well as the phenolic compound depleted extract ($OWE^{øPC}$) were investigated against uropathogenic *Escherichia coli* (UPEC). OWE was quantified by UHPLC for the content of rosmarinic acid, cichoric acid and caffeic acid. 4- and 7-day pretreatment of Balb/c mice with OWE (750 mg/kg) prior to the transurethral infection with UPEC NU14, reduced bacterial bladder colonization. Also, 3- and 5-day posttreatment of Balb/c mice with OWE (750 mg/kg) after transurethral infection with UPEC CFT073, reduced the bacterial load in bladder and kidney, similar to norfloxacin. *In vitro* investigations indicated that OWE (≤ 2 mg/ml) has no proliferation-inhibiting activity against different UPEC strains as well as against T24 bladder and A498 kidney cells. Under *in vitro* conditions, OWE and $OWE^{øPC}$ both exerted a dose dependent antiadhesive activity against UPEC strains NU14 and UTI89. OWE reduced the gene expression of *fimH*, but significantly increased the expression of the motility/fitness gene *fliC*. Increase of bacterial motility on gene level was confirmed by a changed bacterial phenotype by an increased bacterial motility within soft agar assay. OWE also inhibited the bacterial *quorum sensing* in a concentration-dependent manner. Transcriptome analysis by next generation sequencing and cross-validation of data obtained by RT-PCR indicated that $OWE^{øPC}$ down-regulated the genes responsible for chaperone-mediated protein folding/unfolding and pilus assembly process (leading to decrease of porin activity) while flagellar assembly responsive genes were up-regulated as claimed by mRNA-Seq analysis. Thus, it was concluded that OWE transforms the sessile lifestyle of bacteria to a motile one and therefore disables the bacterial surface attachment.

II) A hydroalcoholic extract (1:1) from *Apium graveolens* L. fruits, known as celery seeds (CSE), was characterized by UHPLC/+ESI-QTOF-MS and dominated by the presence of different luteolin-glycosides and related flavon derivatives besides furocoumarins. CSE had no cytotoxic effects against

UPEC strain NU14 and T24 bladder cells within the tested concentration range (0.1 to 1 mg/mL). CSE exerts a dose dependent antiadhesive activity against UPEC strains NU14 and UTI89 under *in vitro* conditions. CSE inhibited bacterial *quorum sensing* in a concentration dependent manner. 4- and 7-day pretreatment of Balb/c mice with CSE (200 and 500 mg/kg/day), transurethrally infected with UPEC NU14, significantly reduced the bacterial load in bladder tissue. Therefore, CSE is evaluated as a strong antiadhesive plant extract for which the traditional use in phytotherapy for UTI might be justified.

III) The rhizomes from *Agropyron repens* (L.) Beauv. were extracted with solvents of different polarities. The extracts did not show any cytotoxic effects against different *E. coli* strains (2980 and NU14) and human T24 bladder cells under *in vitro* conditions. Significant antiadhesive activity against the bacterial attachment to human T24 bladder cells was found for the acetone extract (AAE) at concentrations > 250 µg/mL. Other hydrophilic extracts did not influence the bacterial attachment to the eukaryotic host cells. Bioassay guided fractionation of AAE led to the identification of (E)-hexadecyl-3-(4-hydroxyphenyl)-acrylate (Compound **A**) as the responsible compound for inhibiting the bacterial adhesion to T24 bladder cells. **A** and two other structural analogs **B** (with shorter alkyl chain, C_8) and **C** (with changed phenyl ring system) were synthetized. **A**, **B** and **C** were tested for their potential antiadhesive activity but only **A** reduced the bacterial adhesion significantly, indicating that a shorter alkyl chain at the ester moiety as well as the lack of hydroxylation of the phenyl moiety will abolish the antiadhesive activity. **A** also reduced the bacterial invasion into the T24 bladder cells as shown by a specific gentamicin protection assay.