Summary

The medicinal use of Nasturtium, *Tropaeolum majus* L., is an alternative to antibiotic treatment of urinary and respiratory tract infections. The main antimicrobial agent of *T. majus* is benzylisothiocyanate (BITC), which evolves from glucotropaeolin by enzymatic catalysis after plant tissue damage. The present study aimed at the elucidation of other potentially active compounds from *T. majus* extract. Therefore, the metabolic profile of *T. majus* had to be characterized in detail.

64 constituents have been characterized in a mixed sample of different hydro-methanolic extracts of *T. majus*. Besides glucotropaeolin, compounds belonging to the following classes have been identified by UPHLC-qTOF-MS: amino acids, anthocyanins, carbohydrates, fatty acids, flavonoids, glycolipids, hydroxycinnamic acid derivatives, lysophosphatidylcholines and 13 *N*-phenylpropenoyl-amino acid amides. The cyanogenic glucoside prunasin and its degradation product prunasinamide have been identified in *T. majus* for the first time by comparison with reference compounds. Bretschneiderazine A, 1,3-dibenzylurea, and macaridine, also known from other species of the *Brassicales* order, were tentatively identified for the first time in *T. majus* on the basis of UHPLC-qTOF-MS data.

Detailed investigations on *T. majus* at different developmental stages and harvest times showed distinct metabolic profiles. After drying at 40 °C, the resulting material had greater amounts of thermolabile malonylated flavonoids and glucotropaeolin, whereas plants dried at 80 °C contained increased amounts of macaridine, lysophosphatidylcholine C18:2, and glycolipids.
The influence of the harvest date on the metabolic profiles was explicable by the occurrence of different plant organs. Plants before flowering (ZI) showed increased amounts of compounds such as glycolipids, quercetin-malonylhexosides, and diacylglycerosides that were most concentrated in the leaves. Flowering plants (ZII) showed signals typical for the buds and flowers such as myricetin- and kaempferol-hexoside. Plants with fully developed fruits and residual buds and flowers (ZIII) rarely displayed organ-specific signals.

Unfermented hydro-methanolic extract (TM-1) and fermented, but BITC-free hydro-methanolic extract (TM-2) had no antiproliferative effect against uropathogenic *Escherichia coli* (UPEC) NU14, *E. coli* 2980, *Pseudomonas aeruginosa* ATCC 9027 and 27853 *in vitro*. The extracts had no negative effect on the biofilm formation of both *P. aeruginosa* strains *in vitro*. Biofilm formation of a modified *E. coli* Top10 was inhibited at 2000 µg/mL extract

concentration by about 80% (TM-1 and TM-2), which could not be explained completely by the inhibition of *quorum sensing* of this bacterial strain by about 20% (TM-1 and TM-2).
Inhibition of bacterial adhesion to T24 bladder cells of UPEC NU14 by about 45% (TM-1) and 60% (TM-2) during preincubation of bladder cells with 2000 µg/mL extract demonstrated an influence on host cells *in vitro*. The 50% inhibited invasion of UPEC NU14 into T24 bladder cells after treatment with 1500 µg/mL TM-1 indicated under *in vitro* conditions an additive effect of inhibition of adhesion (approx. 30% for 1500 µg/mL) and invasion (approx. 50%). Incomplete remixing of TM-1 fractions resulted in knockout (KO) fractions, which exhibited an *in vitro* antiadhesive effect against UPEC NU14 (KO-K: approx. 50-65%, KO-RP: approx. 40-60% und KO-S: approx. 25-40%). One particular fraction of TM-1 (lipophilic fraction RP-12) inhibited the adhesion of UPEC NU14 by about 20% (25 µg/mL). Subfractions obtained from this antiadhesive fraction caused a more cytotoxic effect against bladder cells. Coincubation of *E. coli* 2980 with 2000 µg/mL extract together with T24 bladder cells resulted in strong *in vitro* inhibition of adhesion of this bacterial strain (TM-1: approx. 55%, TM-2: approx. 70%).
Both extracts (500-1000 µg/mL) inhibited NO-release of LPS-stimulated RAW 264.7 macrophages by about 20-40% (TM-1) and 35-55% (TM-2) under *in vitro* conditions. Different KO fractions suppressed NO-release by 10-35% (KO-K) and 10-40% (KO-RP). No influence of the extract was observed on the phagocytosis of RAW 264.7 macrophages.

In summary, the results for TM-1 and TM-2 indicate a weak inhibition of adhesion, invasion and biofilm formation of different *E. coli* strains. In this regard, fermented extract TM-2 had a better effect than unfermented extract TM-1. The concomitant compounds - all compounds other than benzylisothiocyanate - seem to have only a minor effect on the bioactivity of *T. majus*.