

**Table S1.** Antibacterial activity (zone of inhibition in mm) of oregano honey samples against *H. pylori* strains isolated from clinical samples (ulcers = 6, gastritis = 8) and a reference strain (*H. pylori* DSM21031).

| Strain      | Concentration of Honey (% v/v) |                              |                            |                              |                            |
|-------------|--------------------------------|------------------------------|----------------------------|------------------------------|----------------------------|
|             | 75                             | 50                           | 25                         | 12.5                         | 6                          |
| <i>HpU1</i> | 27.26 ± 6.4 <sup>ab</sup>      | 22.28 ± 6.3 <sup>abc</sup>   | 15.2 ± 6.9 <sup>ab</sup>   | 6.56 ± 3.4 <sup>a</sup>      | 3.16 ± 1.7 <sup>a</sup>    |
| <i>HpU2</i> | 21.45 ± 5.1 <sup>ab</sup>      | 18.63 ± 4.14 <sup>ab</sup>   | 13.8 ± 3.9 <sup>a</sup>    | 7.7 ± 3.1 <sup>a</sup>       | 2.41 ± 1.28 <sup>a</sup>   |
| <i>HpU3</i> | 15.38 ± 3.3 <sup>a</sup>       | 14.36 ± 3.9 <sup>a</sup>     | 12.18 ± 2.9 <sup>a</sup>   | 9.18 ± 2.2 <sup>ab</sup>     | 5.14 ± 2.1 <sup>ab</sup>   |
| <i>HpU4</i> | 22.48 ± 4.81 <sup>ab</sup>     | 18.16 ± 3.56 <sup>ab</sup>   | 13.3 ± 3.45 <sup>a</sup>   | 9.19 ± 3.39 <sup>ab</sup>    | 3.18 ± 1.2 <sup>a</sup>    |
| <i>HpU5</i> | 29.1 ± 5.1 <sup>ab</sup>       | 21.45 ± 3.1 <sup>abc</sup>   | 18.13 ± 4.3 <sup>abc</sup> | 5.48 ± 4.1 <sup>a</sup>      | 3.5 ± 1.8 <sup>a</sup>     |
| <i>HpU6</i> | 28.78 ± 4.18 <sup>ab</sup>     | 27.15 ± 4.0 <sup>bcd</sup>   | 21.45 ± 3.6 <sup>abc</sup> | 18.13 ± 1.3 <sup>cd</sup>    | 12.14 ± 2.4 <sup>bc</sup>  |
| <i>HpG1</i> | 47.7 ± 4.5 <sup>cd</sup>       | 43.5 ± 4.7 <sup>h</sup>      | 36.26 ± 3.7 <sup>d</sup>   | 30.44 ± 1.6 <sup>e</sup>     | 20.1 ± 2.9 <sup>d</sup>    |
| <i>HpG2</i> | 50.28 ± 4.2 <sup>d</sup>       | 45.88 ± 4.0 <sup>h</sup>     | 26.66 ± 4.6 <sup>bcd</sup> | 15.7 ± 3.9 <sup>abc</sup>    | 5.48 ± 5.4 <sup>ab</sup>   |
| <i>HpG3</i> | 53.44 ± 3.8 <sup>d</sup>       | 32.13 ± 3.9 <sup>cdeg</sup>  | 14.44 ± 2.14 <sup>a</sup>  | 9.90 ± 1.6 <sup>ab</sup>     | 3.78 ± 2 <sup>a</sup>      |
| <i>HpG4</i> | 35.16 ± 4.13 <sup>abc</sup>    | 28.76 ± 3.28 <sup>bcd</sup>  | 18.90 ± 4.2 <sup>ac</sup>  | 13.12 ± 2.45 <sup>abc</sup>  | 4.13 ± 1.1 <sup>a</sup>    |
| <i>HpG5</i> | 44.6 ± 5.51 <sup>cd</sup>      | 42.42 ± 4.5 <sup>egh</sup>   | 34.66 ± 3.9 <sup>bd</sup>  | 27.24 ± 4.4 <sup>de</sup>    | 18.00 ± 4.0 <sup>acd</sup> |
| <i>HpG6</i> | 48.84 ± 5.3 <sup>cd</sup>      | 33.18 ± 3.64 <sup>cdeg</sup> | 29.88 ± 4.18 <sup>cd</sup> | 22.14 ± 4.4 <sup>ce</sup>    | 15.70 ± 3.15 <sup>cd</sup> |
| <i>HpG7</i> | 51.51 ± 5.8 <sup>cd</sup>      | 40.28 ± 4.6 <sup>egh</sup>   | 27.80 ± 4.3 <sup>cd</sup>  | 12.90 ± 3.45 <sup>abcd</sup> | 4.15 ± 2.1 <sup>a</sup>    |
| <i>HpG8</i> | 47.62 ± 3.9 <sup>ad</sup>      | 35.66 ± 4.9 <sup>degh</sup>  | 29.22 ± 4.3 <sup>cd</sup>  | 15.78 ± 3.5 <sup>abc</sup>   | 4.6 ± 1.8 <sup>ab</sup>    |
| Ref         | 51.24 ± 2.4 <sup>d</sup>       | 30.24 ± 1.5 <sup>bcd</sup>   | 15.4 ± 1.1 <sup>ab</sup>   | 10.8 ± 1.3 <sup>abc</sup>    | 1.34 ± 1.1 <sup>a</sup>    |

*HpU1* to *HpU6* are *H. pylori* strains isolated from ulcers, while *HpG1* to *HpG8* are *H. pylori* strains isolated from gastritis. Ref: *H. pylori* DSM21031 (reference strain). Similar superscript letters indicate no statistically significant differences (ANOVA with Tukey's HSD *post hoc* multiple range tests) among the various *H. pylori* strains for the same concentration of honey.

**Table S2.** Antibiotic susceptibility results from six antibiotics against *H. pylori* strains isolated from clinical samples (ulcers = 6, gastritis = 8) and a reference strain (*H. pylori* DSM21031).

| Antibiotic     | <i>HpU</i> | <i>HpU</i> | <i>HpU</i> | <i>HpU</i> | <i>HpU</i> | <i>HpU</i> | <i>HpG1</i> | <i>HpG2</i> | <i>HpG3</i> | <i>HpG4</i> | <i>HpG5</i> | <i>HpG</i> | <i>HpG</i> | <i>HpG8</i> | <i>HpRef</i> | Clinical Breakpoints (mg/L)* |           |
|----------------|------------|------------|------------|------------|------------|------------|-------------|-------------|-------------|-------------|-------------|------------|------------|-------------|--------------|------------------------------|-----------|
|                | 1          | 2          | 3          | 4          | 5          | 6          | 6           | 7           | 6           | 7           | 6           | 6          | 7          | 6           | Ref          | Susceptible                  | Resistant |
| Amoxicillin    | R**        | R          | S          | R          | R          | R          | S           | S           | S           | R           | S           | R          | S          | S           | S            | ≤0.12                        | >0.12     |
| Clarithromycin | R          | S          | R          | S          | R          | R          | R           | S           | S           | S           | S           | S          | S          | S           | S            | ≤0.25                        | >0.5      |
| Metronidazole  | S          | R          | R          | S          | S          | R          | S           | S           | R           | R           | S           | S          | R          | R           | S            | ≤8                           | >8        |
| Tetracycline   | R          | S          | S          | R          | R          | S          | S           | S           | R           | R           | R           | R          | R          | S           | S            | ≤1                           | >1        |
| Levofloxacin   | R          | R          | R          | S          | R          | S          | S           | R           | R           | S           | R           | S          | S          | S           | S            | ≤1                           | >1        |
| Rifampicin***  | R          | S          | R          | R          | S          | R          | S           | S           | R           | S           | R           | S          | S          | S           | S            | ≤1                           | >1        |

\*Proposed by EUCAST (European Committee on Antimicrobial Susceptibility Testing) and the British Society for Antimicrobial Chemotherapy; \*\*R:Resistant, S: Sensitive; \*\*\*Rifampicin was used to screen for rifabutin resistance since rifampicin E-tests are not available routinely (adapted from EUCAST).

**Table S3.** Diameter of the inhibition zones (mm, mean±St. Dev. produced from various solvent extracts (75% v/v) against 14 *H. pylori* strains isolated from ulcers (n=6) or gastritis (n=8) and a reference strain *H. pylori* DSM21031.

| Honey                | <i>HpU1</i> *   | <i>HpU2</i>      | <i>HpU3</i>      | <i>HpU4</i>      | <i>HpU5</i>      | <i>HpU6</i>       | <i>HpG1</i>       | <i>HpG2</i>       | <i>HpG3</i>        | <i>HpG4</i>       | <i>HpG5</i>       | <i>HpG6</i>       | <i>HpG7</i>       | <i>HpG8</i>       | <i>H. pylori</i> DSM21031 |
|----------------------|---|------------------|------------------|------------------|------------------|-------------------|-------------------|-------------------|--------------------|-------------------|-------------------|-------------------|-------------------|-------------------|---------------------------|
| Extract<br>(75% v/v) |   |                  |                  |                  |                  |                   |                   |                   |                    |                   |                   |                   |                   |                   |                           |
| <i>n</i> -Hexane     | 14.35 ± 12.85 ± 14.89 ± 16.41 ± 15.74 ± 16.81 ± 17.38 ± 18.71 ± 17.99 ± 16.9 ± 18.45 ± 17.85 ± 18.4 ± 19.7 ± 18.13 ± 3.5 <sup>a</sup>   | 6.4 <sup>a</sup> | 5.3 <sup>a</sup> | 3.8 <sup>a</sup> | 3.8 <sup>a</sup> | 3.25 <sup>a</sup> | 3.8 <sup>ab</sup> | 4.5 <sup>ab</sup> | 3.7 <sup>ab</sup>  | 3.5 <sup>ab</sup> | 4.3 <sup>ab</sup> | 3.6 <sup>ab</sup> | 3.8 <sup>ab</sup> | 4.2 <sup>ab</sup> | 3.9 <sup>ab</sup>         |
| Diethyl ether        | 22.1 ± 19.5 ± 19.8 ± 19.88 ± 19.8 ± 19.87 ± 23.7 ± 25.1 ± 22.35 ± 25.8 ± 26.4 ± 22.7 ± 22.78 ± 22.74 ± 23.12 ± 5.7 <sup>a</sup>         | 3.7 <sup>a</sup> | 4.7 <sup>a</sup> | 5.3 <sup>a</sup> | 2.9 <sup>a</sup> | 3.7 <sup>ab</sup> | 5.4 <sup>ab</sup> | 4.7 <sup>b</sup>  | 4.7 <sup>a,b</sup> | 4.7 <sup>bc</sup> | 3.1 <sup>b</sup>  | 2.8 <sup>ab</sup> | 3.8 <sup>b</sup>  | 2.7 <sup>b</sup>  | 3.8 <sup>b</sup>          |
| Chloroform           | 14.7 ± 15.4 ± 14.18 ± 15.1 ± 15.78 ± 14.5 ± 12.1 ± 13.24 ± 12.7 ± 13.5 ± 12.8 ± 13.7 ± 12.75 ± 13.7 ± 13.9 ± 5.7 <sup>a</sup>           | 2.8 <sup>a</sup> | 2.9 <sup>a</sup> | 3.9 <sup>a</sup> | 5.2 <sup>a</sup> | 2.8 <sup>a</sup>  | 2.1 <sup>a</sup>  | 3.4 <sup>a</sup>  | 3.8 <sup>a</sup>   | 3.8 <sup>a</sup>  | 2.8 <sup>b</sup>  | 3.8 <sup>a</sup>  | 2.8 <sup>a</sup>  | 2.8 <sup>a</sup>  | 2.8 <sup>a</sup>          |
| Ethyl acetate        | 25.42 ± 23.78 ± 24.58 ± 23.85 ± 25.45 ± 25.05 ± 24.78 ± 27.35 ± 25.78 ± 27.8 ± 25.78 ± 26.58 ± 26.85 ± 26.65 ± 26.35 ± 4.7 <sup>a</sup> | 4.7 <sup>a</sup> | 3.5 <sup>a</sup> | 4.8 <sup>a</sup> | 3.8 <sup>a</sup> | 2.7 <sup>b</sup>  | 6.1 <sup>b</sup>  | 2.1 <sup>b</sup>  | 2.5 <sup>b</sup>   | 1.8 <sup>c</sup>  | 3.2 <sup>b</sup>  | 3.5 <sup>b</sup>  | 2.4 <sup>b</sup>  | 2.5 <sup>b</sup>  | 2.4 <sup>b</sup>          |

\*Strains *HpU1–HpU6* isolated from ulcers and *HpG1–HpG8* from gastritis. Different superscript letters in columns indicate statistically significant differences (ANOVA with Tukey's HSD post hoc comparison,  $p<0.05$ ) in the diameter of the inhibition zone between the solvent extracts within each *H. pylori* strain.

**Table S4.** MIC<sub>95</sub> of solvent extracts (% v/v) of each honey against *H. pylori* strains isolated from ulcers and the reference strain DSM21031.

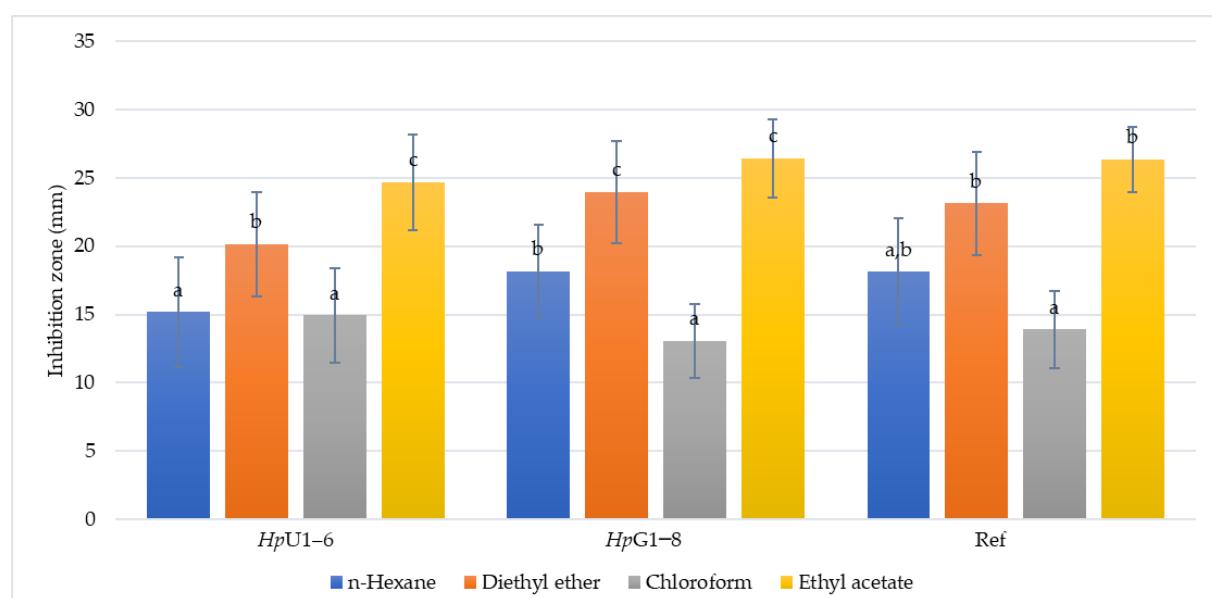
| Solvent          | N* | <i>HpU1</i>                 | N* | <i>HpU2</i>                 | N* | <i>HpU3</i>                  | N* | <i>HpU4</i>                 | N* | <i>HpU5</i>                   | N* | <i>HpU6</i>                 | N* | <i>Hp</i><br>DSM21031      |
|------------------|----|-----------------------------|----|-----------------------------|----|------------------------------|----|-----------------------------|----|-------------------------------|----|-----------------------------|----|----------------------------|
| <i>n</i> -hexane | 32 | 10.23 ± 2.25 <sup>4,c</sup> | 27 | 6.42 ± 4.16 <sup>3,b</sup>  | 7  | 7.78 ± 3.55 <sup>3,bc</sup>  | 11 | 5.97 ± 3.29 <sup>3,ab</sup> | 6  | 5.83 ± 3.41 <sup>2,3,ab</sup> | 9  | 6.38 ± 2.82 <sup>3,ab</sup> | 21 | 4.28 ± 2.45 <sup>3,a</sup> |
| Diethyl ether    | 36 | 3.11 ± 2.84 <sup>1,d</sup>  | 39 | 0.93 ± 0.96 <sup>1,ab</sup> | 41 | 2.13 ± 2.26 <sup>1,c</sup>   | 29 | 0.96 ± 0.65 <sup>1,ab</sup> | 37 | 1.51 ± 1.58 <sup>1,bc</sup>   | 46 | 1.02 ± 0.64 <sup>1,ab</sup> | 48 | 0.52 ± 0.76 <sup>1,a</sup> |
| Chloroform       | 25 | 7.3 ± 2.78 <sup>3,b</sup>   | 22 | 4.26 ± 2.36 <sup>2,a</sup>  | 5  | 5.0 ± 1.76 <sup>2,3,ab</sup> | 12 | 6.83 ± 3.48 <sup>3,b</sup>  | 13 | 6.21 ± 3.68 <sup>3,ab</sup>   | 17 | 6.45 ± 4.07 <sup>3,b</sup>  | 20 | 9.85 ± 2.27 <sup>4,c</sup> |
| Ethyl acetate    | 28 | 4.82 ± 2.03 <sup>2,ab</sup> | 38 | 2.96 ± 2.51 <sup>2</sup>    | 34 | 3.46 ± 3.44 <sup>2,abc</sup> | 33 | 3.35 ± 3.27 <sup>2,ab</sup> | 32 | 3.99 ± 3.24 <sup>2,bc</sup>   | 50 | 2.70 ± 2.80 <sup>2,a</sup>  | 36 | 2.29 ± 1.25 <sup>2,a</sup> |

\* Number of samples with inhibitory effect out of 50 oregano honey tested samples. Different superscript numbers indicate statistically significant differences in rows while superscript numbers indicate statistically significant differences in columns (ANOVA with Tukey's HSD post hoc comparisons at 95%).

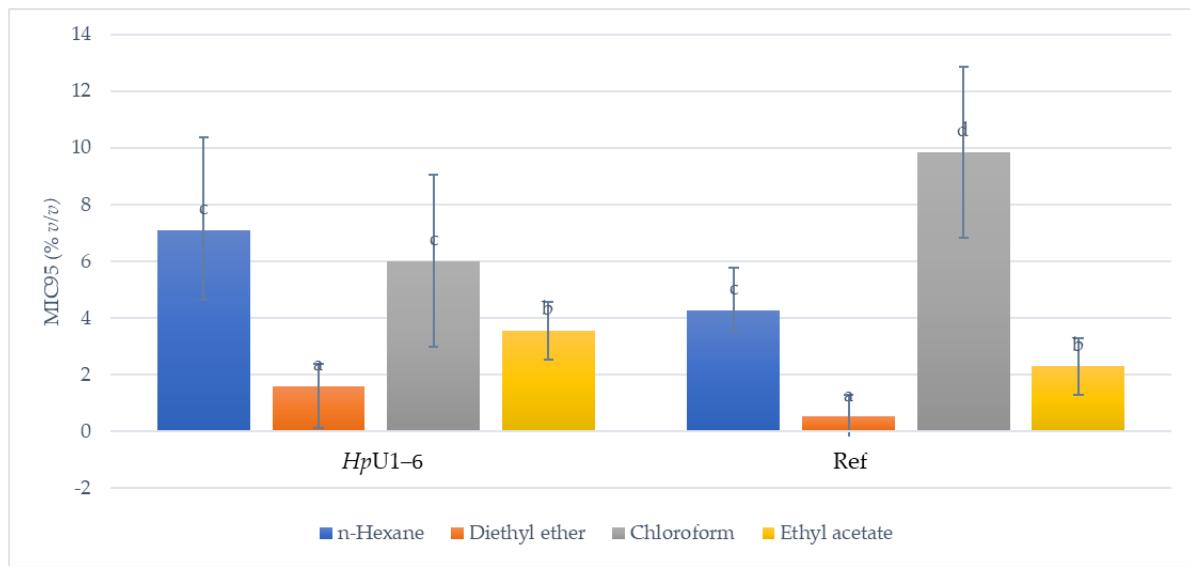
**Table S5.** Urease Inhibitory effect of pure and diethyl ether extracts of oregano honey against two *H. pylori* strains isolated from ulcers (*HpU1*, *HpU2*) and the reference strain DSM21031.

| <i>H. pylori</i> Strain | Oregano Honey         | N* | Effective Concentration (mg/mL) |            |        |
|-------------------------|-----------------------|----|---------------------------------|------------|--------|
|                         |                       |    | Mean ± SD                       | Range      | Median |
| <i>HpU1</i>             | Pure                  | 43 | 91.3 ± 55.8**                   | 12.5–200.0 | 100.0  |
|                         | Diethyl ether extract | 50 | 22.0 ± 18.8                     | 3.0–100.0  | 12.5   |
| <i>HpU2</i>             | Pure                  | 49 | 57.5 ± 40.5**                   | 6.25–200.0 | 50.0   |
|                         | Diethyl ether extract | 50 | 5.93 ± 3.32                     | 1.56–12.5  | 6.25   |
| DSM21031                | Pure                  | 49 | 28.3 ± 18.3**                   | 12.5–100.0 | 25.0   |
|                         | Diethyl ether extract | 50 | 4.43 ± 2.33                     | 1.56–12.5  | 3.125  |

\* Number of samples with inhibitory effect out of 50 oregano honey tested samples. \*\*Statistically significant differences between pure and diethyl ether extract effective concentration according to the Mann–Whitney (Wilcoxon) W-test ( $p<0.01$ ).



**Figure S1.** Mean diameter of inhibition zones from various solvent extracts against ulcer (*HpU1–6*, n=6), gastritis (*HpG1–8*, n=8), and the reference strain of *H. pylori* DSM21031. Different letters above bars indicate statistically significant differences (ANOVA with Tukey's HSD,  $p<0.05$ ) for each group of strains.



**Figure S2.** MIC<sub>95</sub> values (% v/v) of *n*-hexane, diethyl ether, chloroform, and ethyl acetate oregano honey extracts against (6) *H. pylori* clinical strains (*HpU1–HpU6*) isolated from ulcers and a reference strain (*H. pylori* DSM210321). Different letters above bars indicate statistically significant differences (ANOVA with Tukey's HSD,  $p<0.05$ ) for each group of strains.