Susceptibility of *Campylobacter jejuni* and *Campylobacter coli* to Macrolides and Related Compounds

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The susceptibility of 105 thermophilic campylobacters from human and swine origins to eight macrolides and related compounds was tested. Erythromycin, josamycin, clindamycin, and ASE 136 BS (a new erythromycin derivative) were the most active against the human strains. The swine strains were highly resistant, except to pristinamycin. The human *Campylobacter coli* strains (except for two strains) behaved like the *C. jejuni* strains.

*Campylobacter jejuni* and, to a lesser extent, *C. coli*, are now recognized as a major cause of enteric infections of worldwide distribution. Treatment with an antibiotic shown to be effective in vitro can be of value in that it eradicates the campylobacters in the intestine and so prevents a relapse or cross contaminations (especially between children) or both. It also has an effect on the evolution of the disease. The main antibiotic currently used for this purpose is a macrolide, erythromycin, but few studies comparing erythromycin with the other macrolides have been performed. The aim of this study was to determine the susceptibility of *C. jejuni* and *C. coli* to macrolides and the related compounds lincomycin, clindamycin, and pristinamycin as well as to a new compound, ASE 136 BS.

Seventy-nine strains of human origin were tested: 55 *C. jejuni* and 24 *C. coli* isolated in France (32 strains), Vietnam (11 strains), the United States (6 strains), Australia (8 strains), and Hungary (22 strains). Twenty-six *C. coli* strains from swine origin isolated in France (20 strains) and the United States (6 strains) were also tested. All these strains were isolated from fecal samples on a selective medium except for those from Australia, which were isolated by a filtration technique.

The strains were identified by the following characteristics: morphology, oxidase and catalase tests, and growth at 42°C in a microaerophilic atmosphere. The hippurate test was used to differentiate *C. jejuni* (hippurate positive) and *C. coli* (hippurate negative) (10). The strains were maintained frozen at −70°C before being tested. *Staphylococcus aureus* ATCC 25923 was used as a control.

The agents used in this study and their sources were as follows: erythromycin base (Roussel UCLAF, Paris, France), josamycin (Pharmuka, Gennevilliers, France), oleandomycin (Pfizer, Orsay, France), clindamycin and lincomycin chloride (Upjohn, Paris, France), and spiramycin and pristinamycin (Specia, Paris, France). ASE 136 BS is a new macrolide derived from erythromycin (methoxy-2-ethoxy-erythromycylamine acetaldheyde). It is produced by Laboratoires Français de Thérapeutique, Bordeaux, France.

We used the standard agar dilution technique to determine MICs (25). The strains were harvested after 18 h of growth at 42°C, suspended in tryptic soy broth (McFarland 0.5 opacity standard), diluted 1:10, and inoculated onto Mueller-Hinton agar (BioMerieux, Marcy l’Etoile, France) with 5% sheep blood and antimicrobial agent by using a Steers inoculator.

The media were used on the day of their preparation. Reading the plates was performed after 48 h of incubation at 35°C under microaerophilic conditions (85% N₂-10% CO₂-5% O₂). The MIC was defined as the lowest concentration of drug inhibiting any visible growth.

The results are shown in Table 1. Macrolides and related compounds could be divided into two categories according to the MICs for the human *C. jejuni* strains. The most active were josamycin, erythromycin, clindamycin, and the new compound, ASE 136 BS. The others, oleandomycin, spiramycin, lincomycin, and pristinamycin, exhibited less activity. Among the human *C. coli* strains, a bimodal population could be separated, with 22 strains reacting like the *C. jejuni* strains and 2 highly resistant strains (MIC, ≥128 µg/ml) reacting like the swine *C. coli* strains. All the *C. coli* strains resistant at a high level were also resistant to josamycin, clindamycin, and ASE 136 BS, except for two: one was susceptible to clindamycin and ASE 136 BS, and the other was susceptible only to clindamycin.

Pristinamycin seemed to have the same activity against all the strains, in contrast to the other compounds tested.

We did not notice any special behavior for the human strains from different countries. The two highly resistant *C. coli* strains of human origin were from France.

Data concerning the susceptibility of campylobacters to the macrolides or related compounds are scarce. All of the campylobacter-antibiotic studies included erythromycin, which is the most widely prescribed antibiotic for the treatment of campylobacter enteritis, and sometimes clindamycin, but not the others. This results of our study are in agreement with the fact that these two agents are among the most effective. Josamycin was found to be slightly superior to erythromycin, as in the study of Pritivera et al. (G. Pritivera, R. Vaiani, R. Rossi, C. Setti, G. Ortisi, B. Vigo, and M. Bianchi, Proc. 13th Int. Congr. Chemother., p. 21–24, 1983) but in contrast to that of Sticht-Groh and Hof (18). The list of active compounds also contains rosaramycin and SCH 32063 (24), not studied by us, as well as the new molecule, ASE 136 BS, tested in this study.

The other macrolides and related compounds exhibited poorer activity, although pristinamycin was relatively active against highly resistant erythromycin strains, as was reported recently. In a study of the susceptibility of *Campylobacter* spp. from pigs, Gebhart et al. found an MIC of virginiamycin for 90% of *C. coli* strains of 32 µg/ml, whereas that of erythromycin was >128 µg/ml (9).

The percentage of erythromycin-resistant strains is not uniform in the different studies published. It varies from 0%

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TABLE 1. Susceptibility of Campylobacter strains to eight macrolides and related compounds

<table>
<thead>
<tr>
<th>Antimicrobial agent</th>
<th>Human strains C. jejuni (n = 55)</th>
<th>C. coli (n = 24)</th>
<th></th>
<th></th>
<th>Swine strains, C. coli (n = 26)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Range 50%a 90%b</td>
<td>MIC (µg/ml) for:</td>
<td>Range 50%a 90%b</td>
<td>Range 50%a 90%b</td>
<td>Range 50%a 90%b</td>
<td></td>
</tr>
<tr>
<td>Erythromycin</td>
<td>0.5–16 1 8</td>
<td>0.5–2&gt;128 2 32</td>
<td>2-&gt;128 128 &gt;128</td>
<td></td>
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<tr>
<td>ASE 136 BS</td>
<td>0.125–16 1 8</td>
<td>0.25–128 2 32</td>
<td>2-&gt;128 &gt;128</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oleandomycin</td>
<td>0.25–64 16 32</td>
<td>0.5–128 8 32</td>
<td>2-&gt;128 &gt;128</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spiramycin</td>
<td>0.5–128 16 32</td>
<td>4–128 32 &gt;128</td>
<td>2-&gt;128 &gt;128</td>
<td></td>
<td></td>
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<tr>
<td>Josamycin</td>
<td>0.125–16 0.5 4</td>
<td>0.25–128 2 32</td>
<td>2-&gt;128 &gt;128</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pristinamycin</td>
<td>2–64 8 32</td>
<td>4–64 32 &gt;128</td>
<td>8–32 16 32</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lincomycin</td>
<td>1–128 16 64</td>
<td>1–128 32 &gt;128</td>
<td>8–128 &gt;128</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Clindamycin</td>
<td>0.125–16 1 8</td>
<td>0.25–128 8 &gt;128</td>
<td>2–128 128 &gt;128</td>
<td></td>
<td></td>
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</table>

*a* MIC for 50% of strains.  
*b* MIC for 90% of strains.  
*Two strains were susceptible to clindamycin, and one was susceptible to ASE 136 BS.

(1, 2, 3, 5, 14, 17, 26) to 0.4% (20), 1% (12), 2.5% (8), 4.2% (21), 5.3% (7), 8% (22, 23), 10% (11), 11% (15), 12% (13, 18), and 17% (19; Pritiviera et al., 13th Int. Congr. Chemother.). These differences may be related to the method used or to the threshold used to classify a strain as resistant (4 or 8 µg/ml); however, there is also the possibility that the differences may be related to the number of C. coli strains included. In less recent studies, differentiation of the strains on the basis of hippurate hydrolysis was not carried out. All the strains were called C. fetus subsp. jejuni or C. jejuni. We now know that the percentage of C. coli strains isolated may vary widely from one area to another and, therefore, because of their different antibiotic resistance patterns, they can influence the results. In only four studies performed in 1984 (4, 7, 16, 24) was C. coli also included, and in only two studies (18, 24) was the origin of the strains, e.g., swine, well documented.

Our results are in agreement with those of Secker (16), Burridge and Phillips (4), and Wang et al. (24), who found C. coli to be significantly more resistant to erythromycin than C. jejuni, but the human C. coli were not as resistant as the swine C. coli, as we have previously shown (6). We hypothesize that the more highly resistant strains isolated from swine could be the result of exposure of these strains to a macrolide addition in the diet of these animals. This hypothesis is currently under study.

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LITERATURE CITED


