The efficacy of 200 mg oral ofloxacin given twice daily for 3 days was evaluated in 98 hospitalized cases with acute diarrhea or dysentery. Sixty cases were female, most of whom were laborers. Vibrio cholerae, Vibrio parahaemolyticus, Shigella flexneri, Shigella boydii, Shigella sonnei, Aeromonas hydrophila, Aeromonas spp., and Plesiomonas shigelloides were isolated from fecal samples in 36 of 86 cases (42%) with diarrhea and 5 of 12 cases (46%) with dysentery. E. coli agglutinated with various E. coli polyvalent antisera were found in another 25 cases (26%). With the exception of E. coli, most of the clinical isolates were highly susceptible to ofloxacin and norfloxacin with minimal inhibitory concentrations (MICs) of 0.047–0.38 and 0.016–0.25 mg/L, respectively. A total cure was achieved in 96.5% of cases with diarrhea and in 100% of cases with dysentery. There was a delayed response in two cases and only one case clinically failed to respond. V. cholerae was repeatedly isolated on day 3 in another case who had recovered on day 2, and 1 case developed gangrenous cholecystitis and ischemic enteropathy after an initial response to ofloxacin.

**INTRODUCTION**

In Thailand, diarrheal diseases currently afflict almost one million persons, predominantly affecting individuals living in areas where an inadequate clean water supply still exists in addition to poor personal hygiene. Enteric pathogens isolated are similar to those reported from abroad, and recently included V. cholerae O139, which caused the first outbreak in India and Bangladesh. Manifestation of the latter also appeared to be more severe than classical cholera, although DNA sequences of the cholera toxin B subunit gene and multilocus enzyme electrophoresis markers of V. cholerae O139 strains were identical to those of V. cholerae O1 isolates of the seventh epidemic. Treatment is symptomatic, but in severe cases, or in dysentery, antimicrobial therapy may be required. Due to the recent development of multi-drug resistance by enteric bacteria such as Salmonella and Shigella in Thailand, the search for an alternative drug is necessary to cope with the situation.

Fluoroquinolones have been shown to be very active against various enteric pathogens including multi-resistant strains and have proven effective for therapy of bacterial diarrhea, travelers’ diarrhea and resistant V. cholerae infections. In Thailand, ofloxacin is widely available and very inexpensive among the available fluoroquinolones. In this preliminary study, we evaluated the efficacy of ofloxacin therapy in acute diarrhea and dysentery.

**PATIENTS AND METHODS**

**Study design and patient population**

This was an open-label non-comparative trial. Patients gave informed consent before they were consecutively enrolled into the study at Pathumtani community-based hospital during the summer season from February to June, 1995. Inclusion criteria were those who passed watery stool more than 3 times within the previous 24 hours, or at least 1 mucoid bloody stool. The presence of the following excluded patients from the study: age below 15 years old, a history of antimicrobial intake 24 hours before admission, the presence of numerous diarrheagenic intestinal parasites or protozoa, a history of hypersensitivity to quinolones, serum creatinine and transaminases greater than 2 times the normal upper limit, pregnant or breast-feeding women, a clinical suspicion of full-blown AIDS, hypotension that did not respond to rapid fluid resuscitation within 1 hour, stupor or coma at initial admission, or severe vomiting which prevented the oral intake of ofloxacin. Eligible patients were hospitalized until their illness resolved. Ofloxacin (Daiichi Pharmaceutical Co Ltd, Tokyo, Japan) at a dosage of 200 mg twice daily was administered orally for 3 days. Other chemotherapeutic agents were not permitted, with the exception of oral or intravenous fluid...

Key words: ofloxacin, acute diarrhea, dysentery, susceptibility of bacterial enteropathogen
therapy. Cure, delayed response and failure were defined as the disappearance of diarrhea or dysentery on days 1–3, 4–6 and > 6 days after the initiation of therapy, respectively. Complete blood counts, serum creatinine and liver function tests were performed on admission and repeated 7–14 days later.

Culture, identification and MIC determination
Blood cultures were drawn on admission, and stool examinations and cultures were done on admission and day 3, or before discharge if recovery occurred in less than 3 days. A rectal swab and culture was repeated at 7–14 days. Fecal specimens were placed in Cary-Blair transport medium and sent to the laboratory for inoculation onto Mac-Conkey agar, Salmonella-Shigella agar and thiosulfate-citrate-bile salts-sucrose agar. After an incubation of 16–24 hours at 37°C, suspected colonies were identified using BBL Crystal™ Enteric/Nonfermenter ID kit5 (cat. no. 4345000, Becton Dickinson Microbiology Systems, Cockeysville, MD, USA). Shigella species were serologically grouped by their reaction with shigella antiserum polyvalent groups A, B, C and D (Serotest Reagent Inc, Bangkok, Thailand). Salmonella species were grouped using salmonella antiserum polyvalent groups A, B, C, D and E (National Institute of Health, Nonthaburi, Thailand). V. cholerae O1 was serotyped using polyvalent, monospecific antiserum for Inaba, Ogawa and O139 subspecies (Serotest Reagent Inc, Bangkok, Thailand). If no pathogens were suspected and numerous colonies of E. coli were found, we proceeded to detect diarrheagenic E. coli by simple agglutination with E. coli antiserum polyvalent A (O26:B6, O55:B5, O111:B4, O127:B8) and E. coli antiserum polyvalent B (O86:B7, O119:B14, O124:B17, O125:B15, O126:B16, O128:B12) (BBL, Cockeysville, MD, USA). Some strains of E. coli were tested with E. coli O157 antiserum (SA Scientific Inc, San Antonio, TX, USA). The minimal inhibitory concentrations of co-trimoxazole, tetracycline, ofloxacin and norfloxacin for the clinical isolates were determined using E-test strips (AB-Biodisk, Solna, Sweden). The gradient ranges of tetracycline, co-trimoxazole, ofloxacin and norfloxacin were 0.016–256, 0.002–32, 0.016–32 and 0.016–256 mg/L, respectively.

RESULTS
Over the 5-month period, 110 consecutive patients were enrolled, but 12 cases did not complete the study due to early discharge or were lost to follow-up. The remaining 98 cases were evaluable, with 60 female cases (61%). A stool examination disclosed watery diarrhea in 86 cases and dysentery in 12 cases. Blood cultures were negative in all cases. Pathogenic microorganisms were isolated from the stool in 36 of 86 cases (42%) with diarrhea and 5 of 12 cases (42%) with dysentery. Vibrio cholerae (O1 and O139), Vibrio parahaemolyticus, Shigella flexneri, Shigella boydii, Shigella sonnei, Aeromonas hydrophila, Aeromonas spp., Plesiomonas shigelloides and Salmonella group E were found in 13 (1 case, only O139), 10, 4, 3, 2, 4, 2, 2 and 1 cases, respectively. Agglutinable E. coli was found in 25 cases (26%). They were detected with antiserum polyvalent A in 6 cases, antiserum polyvalent B in 10 cases, antiserum polyvalent A and B in 4 cases, antiserum polyvalent A, B and O157 in 2 cases, and antiserum polyvalent B and O157 in 3 cases. These clinical isolates were highly susceptible to ofloxacin and norfloxacin with the exception of E. coli (Table 1). The symptoms of 95 cases (97%) disappeared within 3 days of ofloxacin therapy given at 200 mg twice daily for 3 days (Table 2). One case continued to pass loose stool 3–4 times a day until day 8. A 76-year-old female who recovered in the first 48 hours, developed gangrenous cholecystitis and ischemic enterocolitis 2 days after discontinuation of ofloxacin, and succumbed to septic shock and adult respiratory distress syndrome. V. cholerae O1 was isolated from this case. To investigate whether ofloxacin was beneficial to those who harbored certain enteropathogens, patients were classified into 3 groups according to the microorganisms isolated from their stool. Those with isolated E. coli comprised the first group, the second group consisted of those from whom Vibrio, Shigella, Salmonella, Aeromonas and Plesiomonas were isolated, and patients with negative stool cultures formed the third group. A Kruskal-Wallis one-way ANOVA used to compared the duration of symptoms of each group after treatment showed that there was no statistical significance between the 3 groups with respect to the disappearance of fever (P = 0.1963), abdominal pain (P = 0.2043), abdominal distention (P = 0.6726) and repeated 7–14 days later. Nor were there significant changes in the complete blood counts or blood chemistries of these patients.

DISCUSSION
This study took place during the summer season when there is a higher prevalence of bacterial diarrhea. It is possible that some of the agglutinable E. coli identified in our study were not pathogenic. Currently, four categories of diarrheagenic E. coli are recognized: enteropathogenic, enterotoxigenic, enteroinvasive, enterohemorrhagic, with a new category termed enteroaggregative under current study. A full scale investigation for the isolation of each diarrheagenic isolate is time-consuming and expensive even if only for the isolation of E. coli O157:H7.16 The percentage of agglutinable E. coli isolated gave only a rough estimate and was in agreement with values reported by Begue et al. who noted that the 2 enteropathogens frequently isolated during endemic cholera in the summer season in developing countries were V. cholerae and enterotoxigenic E. coli.17 The result of the susceptibility test also confirmed previous findings in Thailand that most of the