In recent years, new derivatives of rifamide have been developed and tested, particularly rifabutin (RBU) (9) and rifapentine (RPE) (1), which are active on *Mycobacterium tuberculosis* and other medically important mycobacteria (1, 4, 13, 14). We studied their activity against *Mycobacterium leprae* in comparison with the activity of rifampin (RMP).

Mice were inoculated in the left hind footpad (10) with 5 × 10^6 *M. leprae* cells of strain L6382 isolated in 1963 from a patient infected in Rwanda; the isolate had been continuously passaged in our laboratory (7). RBU was a gift from Farmitalia, Milan, Italy; RPE and RMP were gifts from Dow-Lepetit, Milan, Italy. The drugs were solubilized in 75% ethanol, and dilutions were made in tap water. The drugs were administered once at the doses indicated in Table 1 on day 21 postinfection in a 0.5-ml volume administered by stomach gavage.

A control mouse was examined at 6 months postinoculation and thereafter every 28 days. When the number of acid-fast bacilli in the footpad of a control mouse reached 3 × 10^6, four more mice of the control group and five mice of the experimental groups were individually examined, and the number of acid-fast bacilli in their footpads was counted. Counts of 10^6 and more acid-fast bacilli per footpad were considered positive.

In experiment 1 (Table 1), the minimal effective dose (MED) of RMP was 20 mg/kg (body weight), and in experiment 2 it was equal to or lower than 10 mg/kg; in most experiments, the MED of RMP is 20 mg/kg (6, 11). The MED of RBU in both experiments was 2.5 mg/kg, and the MED of RPE was 5 mg/kg or less. In a previous experiment (6), the MED of RPE was 2.5 mg/kg. It may therefore be concluded that in single doses RBU and RPE are eight times more active against *M. leprae* than RMP.

Hastings and Jacobson (5) found that RBU administered continuously in the food was about 30 times more active than RMP. The mechanism of the greater activity of RPE is probably the result of its prolonged half-life as determined both in animals and in humans (1–3). The greater activity of RPE is probably the result of a greater intrinsic activity resulting from increased lipophilicity (9). Studies in humans (11) should determine whether the higher activity of these drugs against *M. leprae* offers advantages in the treatment of human leprosy.

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**LITERATURE CITED**


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