human blood sample containing 500–1000 ppb of triclocarban. These blood samples were prepared by adding known amounts of triclocarban solution in absolute methanol (1.0 μg/μl). Four replicate samples for 500 ppb were spotted on one TLC plate and five replicate samples for 1000 ppb were spotted on another. The average relative standard deviation was 5.2%.

Samples for the radiotracer comparison were prepared by inoculating rabbit blood with a 0.1% methanol solution of ^{14}C-triclocarban. Ten samples ranged from 0 to 5000 ppb. Aliquots of each sample were analyzed for triclocarban using the present method (TLC–UV) and a radioisotope technique with both whole blood and their ether extracts. For isotope analysis, 100 μl of each blood sample was placed directly in 15 ml of 2,5-bis-2-(5,5-butylbenzoxazolyl)thiophene cocktail solution and counted in a liquid scintillation counter[12]. Ether extracts were evaporated to dryness, taken up in 1.0 ml of methanol, and counted in the same manner. The parts per billion values recovered for the unknown samples with three methods are compared in Table I. An analysis of variance (ANOVA test) showed no significant differences in recoveries among the three methods.

This method shows an average 90% recovery from blood with a good correlation with the amounts of triclocarban inoculated in blood. Results of *in vivo* studies with this method with animals following oral intubation and topical application of triclocarban will be published subsequently.

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Clindamycin Phosphate: Neuromuscular and Blood Pressure Effects in Cats

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Abstract □ Three doses (10, 20, and 40 mg/kg) of clindamycin phosphate were tested in each of three feline neuromuscular preparations in a Latin-square sequence, and the muscular responses and blood pressures were compared. No statistically significant dose-related neuromuscular or blood pressure effects were observed.

Keyphrases □ Clindamycin phosphate—neuromuscular and blood pressure effects, cats □ Neuromuscular and blood pressure effects—clindamycin phosphate, cats □ Blood pressure and neuromuscular effects—clindamycin phosphate, cats

Clindamycin phosphate, a semisynthetic antibiotic produced by chlorination of lincomycin, is very similar in structure and antibacterial activity to its parent compound.

Neuromuscular depressive effects of lincomycin were demonstrated in experimental animals using doses comparable to those used clinically (1, 2). Lincomycin has been noted to interact with tubocurarine in a potentially clinically significant fashion to augment neuromuscular depression (3, 4).

Rapid administration of lincomycin has been associated with syncope, hypotension, and cardiac arrest (2, 5, 6).

Because of similarities between these drugs, this pilot experiment, employing the feline neuromuscular preparation, was undertaken to study the potential neuromuscular and blood pressure effects of clindamycin phosphate to determine if further studies were indicated.

Table I—Neuromuscular Effects

Dose, mg/kg	Depression of Time-Tension Integral Response, %
10	24 ± 15
20	15 ± 10
40	40 ± 30

EXPERIMENTAL

Three mongrel cats were anesthetized with halothane, nitrous oxide, and oxygen. A sciatic nerve–gastrocnemius muscle preparation was established as previously described (4, 7). Blood pressure was monitored *via* an arterial cannula and recorded electronically. Each animal received three doses (10, 20, and 40 mg/kg iv) of clindamycin phosphate according to a Latin-square design. Contractions were allowed to return to the control level prior to each administration. The data were examined by analysis of variance and the Student *t* test. The effect of calcium chloride (50 μg/kg) on recovery also was evaluated.

RESULTS

Neuromuscular depression in the cat was produced by all doses of clindamycin phosphate administered. The mean percent depression of the time–tension integral response with 1 *SD* for each dose is shown in Table I. Wide variation between the effects of the

Table II—Blood Pressure Effects

Dose, mg/kg	Depression of Peak Systolic, %
10	15 ± 13
20	20 ± 31
40	29 ± 34

doses occurred; although a dose–response relationship is suggested, an analysis of variance revealed no significant differences in responses among the amount of drug given, the order of dose administration, and the responses of the individual animals to a given dose.

The suggestion of neuromuscular depressive activity prompts one to evaluate statistically muscle depression with control muscle contraction by comparison with the Student t test for significance of depression of all doses given ($0.2 < p < 0.3$). However, with the small number of animals used in this pilot study ($n = 3$) and the variability encountered, it is perhaps not surprising that statistical significance was not achieved. Attempts at reversal of these neuromuscular effects with calcium chloride administered after the nadir failed to alter the pattern of recovery (lincomycin block had been previously shown not to be reversed by calcium) (2).

Depression of peak systolic blood pressure was noted with all but one of the doses given. Mean responses with 1 *SD* (Table II) suggest that this blood pressure effect is dose related; however, an analysis of variance revealed the same lack of significant differences among responses to doses, dose order, and animal studied.

DISCUSSION

The manufacturer recommends that clindamycin phosphate be diluted (6 mg/ml) and administered slowly (not to exceed 1200 mg in any 1-hr period). The dose range is approximately 5–20 mg/kg (8). In this experiment, doses were in this range and also double the maximum recommended dose. Initial clinical studies with clindamycin used intravenously noted no acute neuromuscular depressive or cardiovascular effects (9–11). However, a summary of side effects in more than 1000 patients includes instances of hypertension, hypotension, and cardiac arrest, and the manufacturer warns of possible neuromuscular blocking properties (8). Nevertheless, even with the lack of dilution and the rapid use of up to twice the usual dose, this study revealed a lack of statistically significant dose-related neuromuscular depressive or blood pressure effects in the cat.

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Unexpected Sulfuration Reaction of 1-Substituted Azulenes

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Abstract □ Azulenes reacted unexpectedly and readily with thionyl chloride to give sulfonic acid chlorides and bisthioethers. The sulfonic acids but not the thioethers have antibacterial activity.

Keyphrases □ Azulenes, 1-substituted—reaction with thionyl chloride, antibacterial activity of resulting sulfonic acid derivatives and thioethers □ Antibacterial activity—sulfonic acid derivatives and thioether reaction products of 1-substituted azulenes with thionyl chloride □ Sulfuration reactions—1-substituted azulenes with thionyl chloride, antibacterial activity of resulting sulfonic acid derivatives and thioethers

While preparing some derivatives of azulene *via* Friedel–Crafts acylation (1, 2) using acid chlorides prepared *in situ* with thionyl chloride, the unexpectedly facile reaction of 1-carboxyethylazulene and thionyl chloride was noted. Under the reaction conditions, the primary product was apparently the 3-sulfinic acid chloride, which rapidly disproportionated giving rise to the corresponding bisthioether and sulfonic acid chloride.

The corresponding sulfonic acid is relatively unstable and could not be completely characterized, but its identity was inferred by formation of the more stable amide derivative upon treatment of the anhydrous system with gaseous ammonia. In seeking to confirm the course of the reaction utilizing the more reactive unsubstituted parent compound, azulene, bis(3-chloroazulyl)thioether was separated with difficulty from polymerization products.

The sulfonic acid and sulfonamide show selective