Some of the algal extracts active against both P-388 leukemia and Ehrlich ascites tumor were subjected to preliminary isolation work (Table I). The finding that some of these crude extracts as well as partially purified fractions showed excellent activity at relatively low dosages with no evidence of toxicity is most encouraging.

Table II lists the marine algae that showed a T/C activity of <125% against P-388 lymphocytic leukemia and <20% survivors at 30 days in the Ehrlich ascites tumor system.

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COMMUNICATIONS

Ocular Absorption of Propranolol in Rabbits

Keyphrases □ Propranolol—ocular absorption in rabbits □ β-Adrenergic blocking agents—propranolol, ocular absorption in rabbits □ Absorption, ocular—propranolol in rabbits

To the Editor:

The topical application of β-adrenergic blocking agents to the eye has been found to be effective in the control of glaucoma (1). However, the precise rate and extent of disposition of these compounds in the various ocular tissues have not been fully established. The purpose of this report is to compare and contrast the ocular absorption of a model β-blocking agent, propranolol, to what is known about the widely used miotic pilocarpine.

Male New Zealand albino rabbits, 3.0–3.6 kg, were minimally restrained in wooden boxes; topical and local anesthetics were not used. A 50-μl dose of 0.5% propranolol hydrochloride in isotonic buffer (pH 7.4) was instilled onto the cornea and allowed to distribute normally within the cul-de-sac. All tissue sampling procedures were performed as outlined previously (2, 3). The tissue samples collected were the whole intact cornea, aqueous humor, iris, and lens. The amount and concentration of propranolol in these tissues were determined spectrophotofluorometrically (4). The minimum detection limit for the drug was ~5 ng.

Figure 1 shows the propranolol concentration in ocular tissues as a function of time. The data indicate that propranolol reached a peak concentration in the aqueous humor at ~30 min. This result corresponds well with previous data for pilocarpine, which has a peak time of 20–30 min. This peak time was anticipated in the current studies since it was shown previously that the apparent ocular pharmacokinetic parameters are largely determined by the parallel first-order loss process in the precorneal area, so that most drugs show similar peak times in the aqueous humor (2, 5). The elimination characteristics of propranolol also are very similar to pilocarpine and suggest that both drugs are lost from the eye *via* the same mechanism, namely, aqueous humor turnover. The rate constant associated with this process for pilocarpine in rabbits is 0.017 min^{-1} (2), and this value is nearly identical to the elimination rate of propranolol from the aqueous humor in the present studies (0.019 min^{-1}).

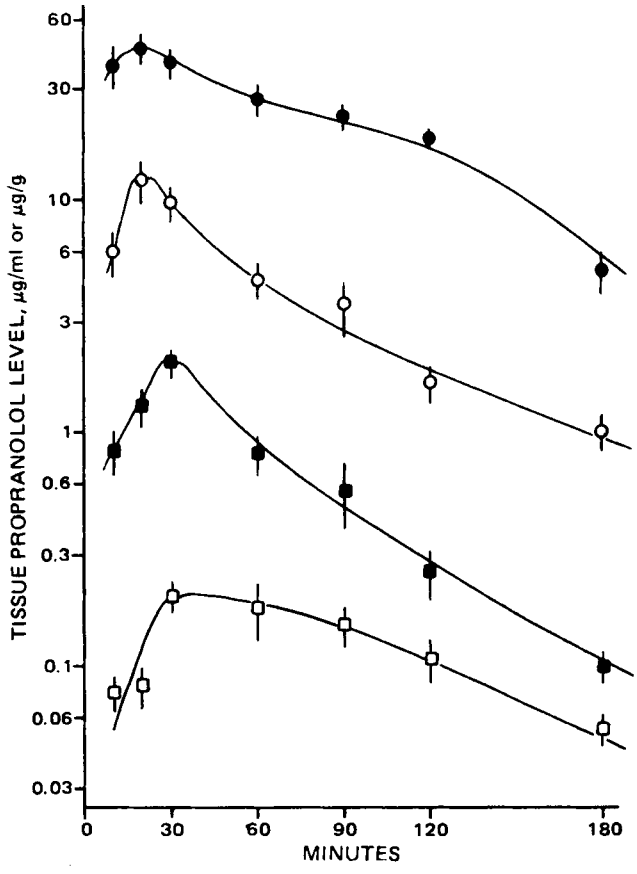

Figure 1—*Concentration of propranolol in various ocular tissues after topical application of propranolol solution. Key:* ●, *cornea;* ○, *iris;* ■, *aqueous humor; and* □, *lens.*

Concentration–time profiles such as those depicted in Fig. 1 can be somewhat misleading in ocular studies of this type which deal with tissues of greatly different distribution volumes. For this reason, it often is useful to consider the amount of drug represented by the peak drug concentration for each tissue. These data are presented in Table I. The rank order for tissue concentration was cornea > iris > aqueous humor > lens, whereas the rank order for tissue amounts was cornea > aqueous humor > iris > lens. The change in rank order for the iris and aqueous humor was due to the 12-fold difference in the wet weights of these

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Table I—Amount of Propranolol Represented by the Peak Concentration in Various Ocular Tissues [a]

Tissue	Peak Concentration, μg/g or μg/ml	Amount of Drug Present in Tissue, μg
Cornea	45.90	3.21
Aqueous humor	2.02	0.61
Iris	12.32	0.31
Lens	0.21	0.06

[a] The weights of the tissues are given in the text.

tissues. The approximate wet weight averages for the cornea, iris, aqueous humor, and lens in the current studies were 70, 25, 300, and 300 mg, respectively.

The relative disposition of propranolol in the various ocular tissues also was different than that of pilocarpine. There was a sixfold difference in peak concentration between the iris and the aqueous humor for propranolol, whereas the two tissues were virtually identical with pilocarpine (3). Furthermore, the penetration into the lens relative to other ocular tissues was greater for propranolol than for pilocarpine. Propranolol is known to act as a local anesthetic and as such may influence membrane permeability. It is unclear whether the differences in tissue distribution for propranolol and pilocarpine can be ascribed wholly, or in part, to this effect.

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Comparative *In Vitro* and *In Vivo* Antifungal Activity of Tolnaftate and Various Undecylenates

Keyphrases □ Antifungal activity—tolnaftate and various undecylenates, comparison *in vitro* and *in vivo* □ Tolnaftate—antifungal activity *in vitro* and *in vivo*, comparison with various undecylenates □ Undecylenates—antifungal activity *in vitro* and *in vivo*, comparison with tolnaftate

To the Editor:

Amsel *et al.* (1) compared the *in vitro* antifungal activity of undecylenic acid and tolnaftate and drew several conclusions. Among these conclusions were: (*a*) the undecylenate product killed the test organisms more rapidly than the tolnaftate-containing product; (*b*) undecylenates possibly are more effective in *in vitro* killing time than tolnaftate alone, and this finding probably applies to the commercial powders; and (*c*) although the concentrations of active ingredients varied in the commercial products tested, the undecylenates probably are more effective (as determined by killing time) than tolnaftate.

Table I—Agar Diffusion Study of Commercial Solutions T [a] and D [a] against Three Dermatophytes

Organism	Contact Time [b]	Zone Size, mm [c] T	D
T. mentagrophytes	1 min	30	0
	5 min	33	10
	15 min	31	11
	30 min	33	11
	1 hr	30	12
	4 hr	33	22
T. rubrum	1 min	42	± [d]
	5 min	20	±
	15 min	35	±
	30 min	41	±
	1 hr	37	±
	4 hr	38	17
E. floccosum	1 min	48	0
	5 min	50	0
	15 min	46	0
	30 min	50	5
	1 hr	47	10
	4 hr	45	10

[a] Commercial solution T contains 1% tolnaftate; commercial solution D contains 10% undecylenic acid. [b] Values between compounds were statistically significant ($p < 0.0001$) at all time points. [c] Using 6-mm disk. [d] These areas showed decreased mycelial growth but were not completely free of growth.

Table II—Agar Diffusion Study of Tolnaftate, Undecylenic Acid, and Zinc Undecylenate against Three Dermatophytes

Organism	Contact Time [b]	Zone Size after Incubation for 96 hr, mm [a] Tolnaftate Solution (0.1%)	Undecylenic Acid [c] Solution (0.1%)	Zinc Undecylenate [c] Suspension (0.1%)
T. mentagrophytes	1 min	29	± [d]	3
	5 min	34	±	8
	30 min	39	13	11
	1 hr	39	18	9
	3 hr	39	27	16
	6 hr	39	30	20
T. rubrum	1 min	43	±	±
	5 min	43	±	9
	30 min	44	18	9
	1 hr	47	25	15
	3 hr	47	33	26
	6 hr	47	>35 [e]	28
M. gypseum	1 min	28	0	0
	5 min	30	±	±
	30 min	37	±	6
	1 hr	38	14	±
	3 hr	39	23	17
	6 hr	39	25	20

[a] Using 6-mm disk. [b] Values between tolnaftate and undecylenates were statistically significant ($p < 0.0001$) at each time point. [c] Average of two disks. [d] These areas showed decreased mycelial growth but were not completely free of growth. [e] Too near edge of plate.

These conclusions were based on the methods, materials, and results of experiments presented in their paper. We have several concerns regarding their unusual methodology, and we therefore question their results and conclusions. We also wish to present *in vitro* and *in vivo* data using standard methods, which show, in contrast to the Amsel *et al.* (1) report, that tolnaftate is superior to the undecylenates. All data were submitted for statistical analysis using an appropriate analysis of variance, Duncan's multiple statistic test, and Fisher's exact test (2).

Our criticisms of the Amsel *et al.* (1) report are as follows:

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