The constituents absorbing at 260 nm were released quickly, and after 45 min further release was observed only when the higher concentrations of phenylethanol were present. At the lowest concentration, phenylethanol had no effect on viability, though there was an increase in leakage. Higher concentrations did have an effect of viability (Fig. 2), but the viable count was still about 10^8 cells ml^{-1} after 4 h.

Best, Best & others (1968) described how vancomycin can be used to detect changes in the integrity of the cell walls of Gram-negative organisms and showed that *P. fluorescens* adsorbs much less vancomycin than *B. subtilis*, but after treatment with sodium edetate uptake of vancomycin by *P. fluorescens* was greatly enhanced. We found that *P. aeruginosa* NCTC 6750, which is normally resistant to vancomycin, after exposure to phenylethanol 0·05 to 0·15% v/v showed increased uptake of vancomycin. Above the higher concentration of phenylethanol, uptake was only slightly increased. With an organism susceptible to vancomycin such as *B. subtilis*, 80% of the available vancomycin is taken up; *P. aeruginosa* in the absence of phenylethanol shows no uptake, and a maximum uptake of 26% in the presence of phenylethanol under the same conditions.

These results indicate that phenylethanol has an effect on the cell envelope of *P. aeruginosa* and supports the hypothesis of Richards & others (1969) that a combination of phenylethanol and a bactericide may enable higher concentrations of the bactericide to enter the cell than would enter in the absence of phenylethanol.

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June 5, 1973

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Effects of dopamine receptor stimulation and blockade on Ro 4-1284-induced enhancement of electroshock seizure

Recent investigations have indicated that dopamine or noradrenaline, or both, are functionally important in convulsive seizure mechanisms. For example, Jobe, Picchioni & Chin (1973) reported that noradrenaline is a modulator of audiogenic convulsions, and Azzaro, Wenger & others (1972) suggested that the reserpine-induced reduction of electroshock seizure threshold is related to a reduction of brain catecholamines and 5-hydroxytryptamine (5-HT). Furthermore, De Shaepdryver, Piette & Delaunois (1962) and Billiet, Bernard & others (1970a, b) have presented data indicating that electroshock seizure threshold in rabbits is regulated by the level of brain dopamine. The present investigation provides additional evidence that dopamine is an important modulator in electroshock seizures.

The electroshock seizure pattern (either clonic or tonic) in Sprague-Dawley female (120–180 g) rats was used to test the effects of selected drugs. Since the tonic pattern is more intense than the clonic pattern (Woodbury & Esplin, 1959; Swinyard, 1963), drugs which increase the incidence of tonus obviously enhance seizure intensity, whereas drugs which decrease the incidence of tonus diminish seizure intensity.

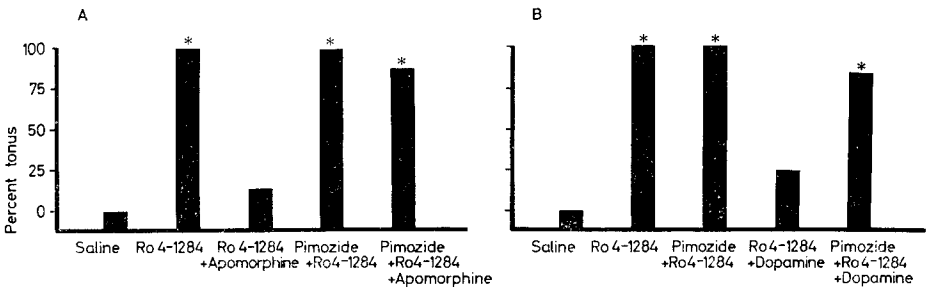

FIG. 1. Effect of pimozide and (A) apomorphine or (B) dopamine on Ro 4-1284-induced enhancement of electroshock seizure. The elapsed time from the initial injection to electroshock administration was 2·5 h. In animals which received all three drug treatments, pimozide (10 mg kg^{-1}, i.p.) was administered as the initial injection at 0 h, Ro 4-1284 (10 mg kg^{-1}, s.c.) was administered as the second injection at 0·5 h, and apomorphine (10 mg kg^{-1} i.p.) was administered as the third injection at 2·25 h(A), or dopamine HCl (1200 μg, calculated as the free base, intracerebroventricularly) was administered as the third injection at 2·0 h(B). Animals which did not receive pimozide, Ro 4-1284 and/or apomorphine or dopamine were injected with saline by appropriate routes and time schedules such that they were handled and treated in the same manner as animals receiving all three drugs. Eight animals were used per group. The symbol * indicates a significant ($P < 0.001$) difference from the saline-control mean as determined by the chi square test.

Similar methods of assessing seizure intensity have been used by Prockop, Shore & Brodie (1959) and De La Torre & Mullan (1970).

Electroshock seizures were induced by stimulation of each animal with 26 mA at 110 V for 0·2 s through corneal electrodes. This procedure routinely produced only clonic seizures in control (saline-treated) animals. Drugs used in the present study are known to produce alterations in brain dopamine levels or to stimulate or block brain dopamine receptors. Ro 4-1284 (2-hydroxy-2-ethyl-3-isobutyl-9,10-dimethoxy-1,2,3,4,6,7-hexahydro-11bH-benzo[a]quinolizine), a short-acting reserpine-like catecholamine-depleting agent, was administered subcutaneously. Pimozide, a dopamine receptor blocking agent (Andén, Butcher & others, 1970) and apomorphine, a dopamine receptor stimulating agent (Ernst, 1967) were administered intraperitoneally. Dopamine HCl was injected into the right lateral ventricle of the brain according to the technique of Grunden & Linburn (1969).

Fig. 1A and B shows that Ro 4-1284 produced a marked enhancement of seizure intensity within 2 h after its administration, a time when brain dopamine and noradrenaline are severely depleted in rats (Jobe & others, 1973). In contrast, central dopamine receptor stimulation by apomorphine (Fig. 1A) or by the intracerebroventricular injection of dopamine itself (Fig. 1B) completely antagonizes the enhancing effects of Ro 4-1284. However, pretreatment with pimozide, a dopamine receptor blocking agent, effectively prevents both the apomorphine- and the dopamine-induced antagonizing effects.

These findings indicate that an increase in central dopamine activity diminishes seizure intensity whereas a decrease in such activity enhances seizure intensity. Since pimozide specifically blocks central dopamine receptors (Andén & others, 1970), our results indicate that the seizure diminishing actions of dopamine and apomorphine result from a specific dopamine receptor effect. These observations lend further support to the concept that endogenous dopamine exerts an inhibitory effect on electroshock seizure (De Shaepdryver & others, 1962; Billiet & others, 1970a, b).

This work was supported by a grant from the Pharmaceutical Manufacturers Association Foundation, U.S.A.

We are grateful to Dr. Paul A. J. Janssen of Janssen Pharmaceutical (Beerse, Belgium) for the pimozide and to Dr. W. E. Scott of Roche Laboratories (Nutley, New Jersey, U.S.A.) for the Ro 4-1284. Apomorphine and dopamine HCl were purchased

from Merck and Co. (Rahway, New Jersey, U.S.A.) and Regis Chemical Co. (Chicago, Illinois, U.S.A.), respectively.

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Nuclear magnetic resonance studies of cetomacrogol 1000 - benzaldehyde - propyl gallate interactions

The system cetomacrogol 1000–benzaldehyde–propyl gallate–water has been examined by nuclear magnetic resonance spectroscopy.

The work was confined to aqueous systems containing 10% cetomacrogol and propyl gallate and benzaldehyde in concentrations which give clear solutions. These solutions contain spherical micelles and correspond to the L1 systems discussed by Nixon, Ul Haque & Carless (1971).

Spectra were obtained using a Varian T-60 high resolution spectrometer equipped with Perma-lock, T-6055, operating temperature of the probe was 35°.

Chemical shifts were measured by expanding the field to 50 Hz per chart width and are quoted with respect to the positions of the corresponding signals of 10% cetomacrogol 1000 in water.

Details of the experimental techniques, susceptibility corrections and accuracy were described previously (Jacobs Anderson & Watson, 1971).

Nixon & others (1971), from their studies of a series of phase diagrams of the cetomacrogol 1000–water–benzaldehyde–propyl gallate system, found that the solubilization of benzaldehyde by the cetomacrogol micelles was decreased by the addition of propyl gallate. These workers postulated that the decrease in solubility may be the result of competition by the benzaldehyde and propyl gallate for the same binding sites.

Fig. 1 (a) shows that both the polyethylene oxide proton signal and the alkyl methylene proton signal shift to higher fields upon the addition of propyl gallate to solutions of 10% cetamacrogol in water. The shift for the alkyl methylene protons is initially slightly greater than that for the polyethylene oxide protons. The shift