1398. PHARMACOLOGIC STUDY OF A NEW ORGANIC NITRATE AND MECHANISM OF ACTION OF THIS CLASS OF DRUGS. R. H. Buller* and C. Jelleff Carr. Dept. of Pharmacology, Purdue Univ. School of Pharmacy, Lafayette, Ind.

Alpha-methyl-D-glycopyranoside tetranitrate (methyl glucoside tetranitrate), the first member of a new series of organic nitrates, has been studied pharmacologically. This drug, when suspended in Methocel and introduced orally in doses ranging from 30 mg/kg to 60 mg/kg, was found to lower the blood pressure of both normotensive and hypertensive rats. When administered intraduodenally in 30 mg/kg to 50 mg/kg doses to dogs under ether anesthesia, a depressor response was elicited within 15 min. Intravenous introduction of molecular equivalent doses of methyl glucoside tetranitrate and erythrol tetranitrate in etherized dogs produced nearly identical depressor responses. No methemoglobinemia was observed in dogs after intravenous and intraduodenal doses. The oil-water distribution coefficient of methyl glucoside tetranitrate and other organic nitrates was investigated. The possible correlation of the findings to depressor potency will be discussed. There were no observable toxic effects from 200 mg/kg doses of methyl glucoside tetranitrate after i.v. or i.p. introduction in rats or oral introduction in rabbits. A study of the distribution of radioactive phosphorus-32 in cardiovascular tissue of normotensive rats was made and compared to that found in hypertensive rats. A lower phosphate uptake was observed in the heart and ear tissues of the hypertensive animals. The radioactive phosphorus-32 uptake of the tissues of the heart and ear of normotensive animals pretreated with erythrol tetranitrate was significantly greater than that seen in non-nitrate treated animals.

1399. EFFECT OF CHLORPROMAZINE ON BLOOD ALCOHOL LEVEL. T. N. Burbridge, Dale Tipton,* V. C. Sutherland* and A. Simon.* Depts. of Pharmacology and Psychiatry, Univ. of California School of Medicine, San Francisco.

During a metabolic study of problem drinkers, it was observed that chlorpromazine increased the blood alcohol level. To analyze the cause, a study was carried out using rabbits. Animals were given 2 gm/kg of 20% ethanol orally. Cardiac blood samples were taken at 15 and 40 min for duplicate alcohol determinations. The animals were then treated with 3 mg/kg of chlorpromazine subcutaneously twice daily for a week and the procedure repeated 1-1/2 hr after the last dose. The mean blood levels for untreated and treated were 1.04 and 1.50 mg/ml respectively at 15 min ($P < .001$) and 1.22 and 1.50 respectively at 40 min ($P = .02$). Similar values were obtained whether the animals were fed or starved. To assess the role of absorption, 1 gm/kg of alcohol was given i.v. in exactly 5 min and blood samples were taken as before. The mean blood levels of untreated and treated were 1.14 and 1.27 respectively at 15 min ($P = .04$) and 0.98 and 1.09 respectively at 40 min ($P = .06$). Reserpine, phenobarbital and saline treated controls did not demonstrate this effect. It was found that a single dose of chlorpromazine caused the same effect. (Supported in part by the Alcohol Rehabilitation Comm. of California.)

1400. ELECTRORETINOGRAPHIC EFFECTS OF LSD-25, BROM-LSD AND LSM (LYSERGIC ACID MORPHOLIDE). H. M. Burian,* W. J. Fleming* and R. M. Featherstone. Depts. of Ophthalmology and Pharmacology, College of Medicine, State Univ. of Iowa, Iowa City.

Rabbits comfortably immobilized in a light-tight electrically-shielded box were used. Specially designed featherweight corneal electrodes and indifferent forehead electrodes provided leads for recording electroretinograms in response to light flashes occurring every 4 sec. Dim constant background illumination was provided. ERG, EEG and EKG were continuously recorded. Two Harvard multiple-speed infusion pumps connected through polyethylene tubing to the marginal ear vein of the animal in the box were used to administer compounds at a uniform rate. Thus continuous records were obtained for the total dose ranges of the compounds investigated. The responses of LSD-25-treated rabbits to sub-maximal stimuli were shown to be greater in voltage than controls. They also appeared to be similar in shape to responses elicited by maximal stimuli. Brom-LSD had no effect. The interrelationships as demonstrated by this technique of the LSD-induced responses to those obtained with Brom-LSD, LSM, serotonin and other compounds, given alone or in combination, will be discussed. (Work supported by grants B-349 and B-615, NIH.)

1401. COMPARISON OF DOSE DEPENDENT EFFECTS OF NALORPHINE WITH THOSE OF LEVALLORPHAN IN PRODUCTION OF GRADED ABSTINENCE IN MORPHINE DEPENDENT MONKEYS. R. H. Burns,* D. A. McCarthy,* G. A. Deneau* and M. H. Seevers. Dept. of Pharmacology, Univ. of Michigan, Ann Arbor.

Fifteen monkeys, physically dependent on 3 mg/kg q6h of morphine sulphate, were used in this study. During a series of 14 experiments, conducted at 3- to 5-day intervals, each animal received 6 doses of nalorphine (0.0125-0.4 mg/kg) and 6 doses of Levallorphine (levo-3-hydroxy-morphinan tartrate) (0.0063-0.2 mg/kg). Untreated control animals were also observed. The experimenter administered the drug in a randomized pattern so that each animal received each dose of each drug once with the grading of effects being performed by a second observer on a blind basis. The animals were observed for 3 hr and graded just prior to and at 1/2-, 1-, 2- and 3-hr intervals following injection. The resulting abstinence syndromes were graded according to intensity on an 8 grade scale (Irwin and Seevers, Fed. Proc. 13:369, 1954). Comparison of the resulting parallel log dose-effect curves shows Levallorphine to be about 3 times as potent as nalorphine in its ability to produce abstinence signs in morphine dependent animals. It may be concluded that both of these antagonists act similarly in producing the acute abstinence syndrome, and that over a suitable dose range the intensity of withdrawal is proportional to the dose of antagonist used.