minations of glyceryl trinitrate in the present U.S.P. adsorbate and in tablets. The results, given in Table III, agreed within 1.0% of the averages of results obtained by the nitrate reduction, infrared, and colorimetric methods. In general, the recoveries of glyceryl trinitrate from the tablets agreed within 3% of the amounts determined by the phenoldisulfonic acid colorimetric procedure (4), as given in Table IV.

In infrared spectrophotometry, it is preferable to compare a sample directly with the reference standard. However, secondary standards are useful when the reference standard is unstable, difficult to obtain or maintain, or otherwise presents a problem. This present use of benzoic acid in analyses of glyceryl trinitrate is one example of the application of a secondary standard in quantitative analyses.

The method is rapid and allows final identification of the analyzed material by its infrared spectrum.

SUMMARY

A method is presented for the infrared analysis of glyceryl trinitrate using benzoic acid as a secondary standard. In general, the results of analyses agreed favorably with those obtained by the U.S.P. nitrate reduction, by an infrared spectrophotometric method using a glyceryl trinitrate adsorbate standard, and by a phenoldisulfonic acid method.

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Promazine Hyperthermia in Young Albino Mice

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The intraperitoneal administration of promazine hydrochloride to albino mice at a dosage level of 1 mg./Kg. of body weight caused hyperthermia in 10-day-old and hypothermia in 38-day-old animals. The removal of the chlorine atom from the structure of chlorpromazine decreased significantly the hyperthermic and hypothermic responses of the phenothiazine in immature and mature mice, respectively. No significant difference due to sex was noted in the activity of the drug at different ages.

DURING THE pioneer pharmacologic investigation of chlorpromazine, Courvoisier and her coworkers (1) observed that the phenothiazine caused a profound fall in body temperature in mature animals, a response that has been confirmed since in a wide variety of species, including man (1–5). Recently, this laboratory demonstrated that the effect of chlorpromazine on the body temperature of mice was influenced by age, for the drug elicited a significant hyperthermia in 10-day-old and hypothermia in 35- and 38-day-old animals (6).

Promazine, the dechlorinated analog of chlorpromazine, is qualitatively similar to the parent compound in its biological behavior, although quantitatively it is generally assumed to be less potent. Because many phenothiazines including promazine, are known to induce hypothermia in adult mammals, the purpose of this study was to ascertain whether the effects of promazine in immature mice were also influenced by age and, if so, to what extent.

EXPERIMENTAL

Albino mice (1140) (Huntingdon Farms, Inc., HTF strain) were divided into six groups, each containing from 119 to 238 animals, according to the following ages: 10, 15, 20, 25, 30, and 38 days. The age difference of mice within a group did not vary more than 15 hours. Except for the youngest age groups (10 and 15 days), each group was equally divided regarding sex. Food was withdrawn 15 minutes and water 1 hour before experimentation to provide for nutritional constancy. Immediately after weighing each mouse on a triple-beam Ohaus balance, the animal was confined in a 100-ml. glass beaker with a screen top and kept at a constant environmental temperature of 38° 15 minutes before injection and throughout the 30-minute observation period. Temperature recordings were taken orally to the nearest 0.1° immediately prior to and 30 minutes after each injection with a model 43 Tele-Thermometer equipped with a No. 402 probe.[1] Freshly prepared aqueous solutions of promazine hydrochloride[2] were administered at a dosage level of 1 mg./Kg. to one-half of a group (equally divided regarding sex), while the remaining mice received distilled water[3] and served as controls. All injections were intraperitoneal at a fixed volume of 0.1 ml.

The significance of difference between the means of drug and control temperatures was estimated by the *t* test, and probability levels were also indicated. Probability levels below 95% were designated insignificant.

RESULTS AND DISCUSSION

The effect of promazine hydrochloride, administered intraperitoneally at a dosage level of 1 mg./Kg., on the body temperature of young albino mice, was influenced by age (Table I). Table I shows that the differences between drug and control groups are significant at extremes of age only, and that there is no evidence that the differences in ages 20 through 30 days could not have occurred by chance. In two-hundred and eleven 10-day-old mice of undifferentiated sex, promazine produced an average increase in the oral temperature of approximately

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[1] Yellow Springs Instrument Co., Yellow Springs, Ohio.

[2] Marketed as Sparine by Wyeth Laboratories, Philadelphia, Pa.

[3] Marketed as Water for Injection by the Philadelphia Ampoule Laboratories, Philadelphia, Pa.

TABLE I.—EFFECT OF PROMAZINE ON THE BODY TEMPERATURE OF YOUNG ALBINO MICE

	Mice, No.	Sex	Wt., Gm.	Initial Temp., °C.	Final Temp., °C.	Temp. Change, °C.	Promazine Temp. Change, °C.	t	p
10-Day-old									
Drug	103	...	4.85	33.62	34.67	+1.05	+0.75	7.57	0.001
Control	108	...	5.31	34.01	34.31	+0.30			
15-Day-old									
Drug	59	...	8.28	34.98	34.98	0.00	+0.38	3.53	0.001
Control	60	...	8.52	34.85	34.47	−0.38			
20-Day-old									
Drug	42	M	9.52	35.94	35.82	−0.12	−0.08	0.79	[a]
Control	36	M	9.43	36.07	36.03	−0.04			
Drug	42	F	9.27	36.07	35.95	−0.12	+0.07	0.70	[a]
Control	48	F	9.30	36.08	35.89	−0.19			
25-Day-old									
Drug	42	M	13.77	35.90	35.84	−0.06	+0.03	0.27	[a]
Control	42	M	13.86	36.07	35.98	−0.09			
Drug	42	F	13.88	35.96	36.03	+0.07	+0.04	0.35	[a]
Control	42	F	13.91	36.16	36.19	+0.03			
30-Day-old									
Drug	59	M	17.54	36.47	36.36	−0.11	−0.07	0.71	[a]
Control	60	M	17.73	36.40	36.36	−0.04			
Drug	60	F	17.32	36.46	36.38	−0.08	−0.03	0.26	[a]
Control	59	F	17.43	36.43	36.38	−0.05			
38-Day-old									
Drug	58	M	32.79	36.84	36.52	−0.32	−0.27	2.33	0.05
Control	58	M	29.46	36.70	36.65	−0.05			
Drug	60	F	24.00	37.00	36.73	−0.27	−0.26	2.59	0.02
Control	60	F	23.62	36.54	36.53	−0.01			

[a] No significance.

0.8° over the control group, which received only water.

At 20 days of age, when sexual differentiation was possible, the animals were separated sexually; the results were recorded. At this age, and at 25 and 30 days of age, no significant differences between the mean before and after temperatures were noted in both male and female animals. Therefore, the drug in these age groups had no effect on body temperature.

In one-hundred and sixteen 38-day-old male mice, promazine produced a body temperature drop of slightly less than 0.3° (compared to the controls) which was significant at the 95% level of probability. One-hundred and twenty female mice in this age group showed a fall in body temperature of approximately 0.3°, significant at the 98% level of probability.

These results are quite similar to those elicited by chlorpromazine (6), which demonstrated a dual action on body temperature dependent on age and characterized by a significant hyperthermia in immature mice and a marked hypothermia in mature mice with a period in between where no change occurred. A major difference between the two phenothiazines was observed in the greater degree of activity of chlorpromazine. This potency variation has also been noted in other areas, like psychiatry, where promazine is less effective than chlorpromazine in treating certain mental disturbances (7–9). A qualitative difference in the distribution of these phenothiazines apparently does not exist (10); yet it has been shown that promazine occurs in the brain in a lower concentration than its chlorinated analog (11). It is interesting that Van Proosdij-Hartzema (12) showed that chlorpromazine was more active than promazine in lowering the body temperature of rats, an observation that has been confirmed in this study with 38-day-old mice.

SUMMARY

The effect of promazine on body temperature is influenced by age; the drug causes significant hyperthermia in 10- and 15-day-old mice and hypothermia in 38-day-old mice.

Promazine was less potent than chlorpromazine in altering the body temperature of immature and mature mice.

The quantitative differences which exist between the temperature responses evoked by promazine and chlorpromazine are due to the absence of a chlorine atom in the structure of the former.

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