

activity (steps taken) by the sheep and pigs during 24 hours, and the division of this activity between day and night.

	Day	Night
	%	%
Sheep	2629 (78)	714 (22)
Pig	3130 (88)	386 (12)

The ratio of day to night activity for the pigs is more than twice that for the sheep. How strongly the pig's free activity is conditioned upon daylight is shown by this observation: at the beginning of the experiment when there was light at both 6 A. M. and 6 P. M. the pigs were found moving about the yard at these hours; but toward the end, when it was dark both morning and night, the pigs always had to be roused from sleep.

Two incidental influences upon free activity may be noted. In certain of the female animals there was an opportunity during the course of the experiment to observe the effect of the oestrous cycle. For example, one sow during heat ran 8700 steps in 24 hours as contrasted with an average of 4001 steps for 10 other 24-hour periods when not in heat. A striking manifestation of the sow's hyperactivity was her tendency to run about at night; in the night of the selected 24-hour period during heat she took 2243 steps as contrasted with an average of 346 for 10 other nights. The weather also seemed to have some effect on the activity of the animals. During the 2 coldest nights the sheep and pigs' activity was reduced by nearly 25%.

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Studies in Sympatheticomimicity, III: Physiological Effects of More Non-amino Catechol Derivatives.

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Muhlmann¹ was the first to point out that catechol (3,4-dihydroxy-benzene) produced a rise in the blood pressure of the intact anesthetized rabbit. Dakin² attributed much of the typical action of epinephrine to the catechol nucleus. Later, Barger and Dale³

¹ Muhlmann, *Deutsch. Med. Wochensh.*, 1896, **22**, 409.

² Dakin, *Roy. Soc. Proc. B.*, 1905, **76**, 498.

³ Barger and Dale, *J. Physiol.*, 1910, **41**, 19.

showed that non-catecholic amines produced similar effects; they attributed the action of sympatheticomimetics to the amine group and drew the conclusion that catechol raises the blood pressure by direct muscle stimulation, rather than by sympathetic imitation. Mulinos and Osborne^{4, 5} demonstrated that catechol, ethylcatechol (3,4-dihydroxyphenylethane), acetocatechol (alpha(3,4-dihydroxyphenyl)ethanone), and chloracetocatechol (alpha(3,4-dihydroxyphenyl)betachloroethanone) possess sympatheticomimetic properties in which the inhibitor effects predominate. Mulinos and Osborne⁴ claimed that the catechol nucleus is in great part responsible for the typical sympatheticomimicity of epinephrine, and that the 3,4-position of the phenyl hydroxyls, a 2-carbon sidechain, a beta-carbon hydroxylated, an alpha-carbon hydrogen substituted by some indifferent radical, preferably an amine, and with all of these the levorotatory isomer, were the factors in the formation of a sympatheticomimetic drug.

Weinstein and Manning⁶ stated that monomethylamino-3:4-quinone and monomethylaminoethanol-3:4-quinone, which are adrenalone and epinephrine respectively with the phenyl hydroxyls converted to the quinone form, have no effect upon the blood pressure. Thus destruction of the catechol nucleus has obliterated the vasopressor power, even though the amine and skeleton of epinephrine and adrenalone are still present.

In this paper we report the effects of 6 new compounds upon the blood pressure of the cat. Various modifications of the alpha(3,4-dihydroxyphenyl)ethanone skeleton were synthesized. We have introduced one, 2 or 3 acetyl radicals into the frame in the 3- or 4-hydroxy, 3- and 4-hydroxy positions of the phenyl group, and in both hydroxys and on the beta-carbon of the side chain. We introduced a hydroxy in place of the chlorine in chloracetocatechol. And we introduced one and 2 acetyls in the catechol nucleus.

The compounds thus synthesized were: alpha(3,4-acetoxy-hydroxyphenyl)betachloroethanone, alpha(3,4-diacetoxyphenyl)betachloroethanone, alpha(3,4-diacetoxyphenyl)betaacetoxyethanone, alpha(3,4-dihydroxyphenyl)betahydroxyethanone, 3,4-diacetoxybenzene, and 3,4-acetoxy-hydroxybenzene.

These drugs were tested for blood pressure effects in 10 cats, using epinephrine as a control. No other drugs were injected other than those described in this paper. Chloracetocatechol and catechol were tested in 48 cats. Doses of 2.5 to 10 mg. were given intra-

⁴ Mulinos and Osborne, *PROC. SOC. EXP. BIOL. AND MED.*, 1935, **32**, 1344.

⁵ Mulinos and Osborne, *PROC. SOC. EXP. BIOL. AND MED.*, 1935, **33**, 458.

⁶ Weinstein and Manning, *PROC. SOC. EXP. BIOL. AND MED.*, 1935, **32**, 1096.

venously in the intact cat anesthetized with intraperitoneal nembutal, 40 mg. per kilo, and atropinized with 2 mg. per kilo of the sulfate intramuscularly; both vagi were cut. The rises in pressure varied from 25 to 50 mm. of mercury, depending upon the dosage and drug. Figures 1, 2 and 3 show typical effects for 3 different types of drugs. From this it is seen that acetylation of the phenylhydroxyls does not eradicate the vasopressor power of the alpha (3,4-dihydroxyphenyl)ethanone group, nor of catechol; the blood pressure rise is in no way diminished, if not increased by acetylation.

Conclusion. Ten non-amine catechol derivatives cause a rise in the blood pressure of the intact cat. Acetylation of catechol and the

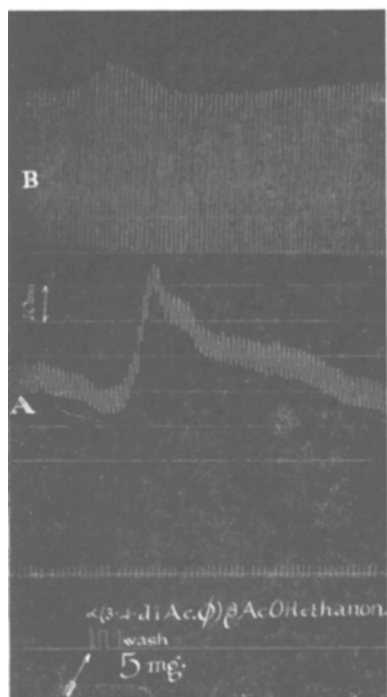


FIG. 1.

FIG. 1.

Effect of alpha (3,4-diacetoxyphenyl) betaacetoxyethanone, 5 mg., on blood pressure (A) and respirations (B) of the intact cat. Neutral solution. All figures reduced four times.

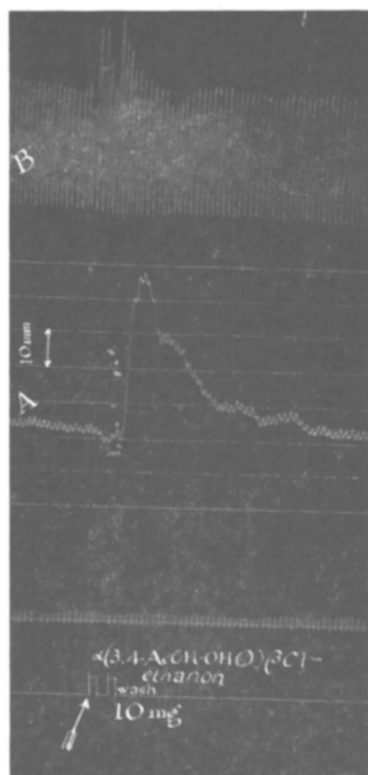
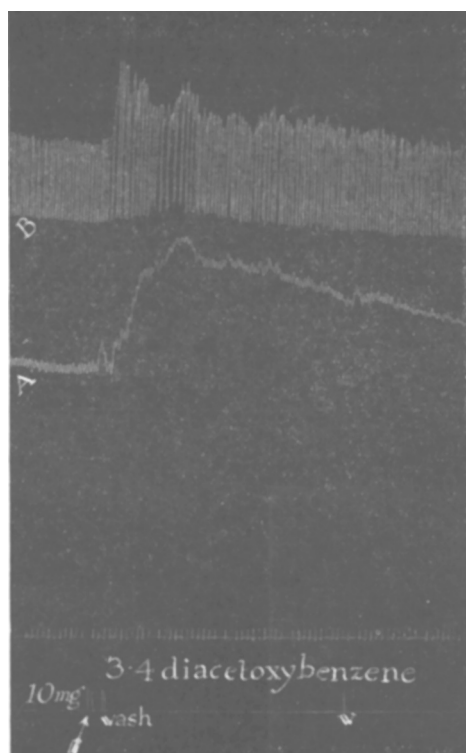


FIG. 2.

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Effect on blood pressure and respirations of 10 mg. of alpha (3,4-acetoxyphenyl) betaachloroethanone; solution neutral to litmus.

**FIG. 3.**

Effect of 3,4-diacetoxybenzene on the blood pressure and respiration; 10 mg. were given.

alpha(3,4-dihydroxyphenyl)ethanone derivatives does not destroy the vasopressor ability. The physiological effects of these drugs on other organs and the effects on the blood pressure of the pithed, decerebrated and demedullated cat are now being studied and will be reported in the near future.