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Antagonistic Action of Dinitrothymol and Dinitrocresol on Cellular Respiration.

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In an extensive study of the biological effects of nitro and dinitrophenols[1] it was found that extremely small concentrations of 2,4-dinitrothymol (1-hydroxy, 3-methyl, 6-isopropyl, 2,4-dinitrobenzene) blocked the cell division of fertilized sea urchin *(Arbacia punctulata)* eggs without, in any concentration, giving more than a slight stimulation of oxygen consumption. This behavior was in marked contrast to that of certain other nitro compounds, including 4,6-dinitrocarvacrol, the isomer of 2,4-dinitrothymol, which displayed a stimulating action on respiration, increasing to an optimum and then progressively disappearing as the concentration of reagent was made larger. These nitro compounds which stimulated respiration also reversibly blocked the cell division of fertilized sea urchin eggs, the initial concentration for division block being just equal to or slightly larger than that producing the optimum respiratory rise.

The results with dinitrothymol suggest that the above outlined effects of 4,6-dinitro-o-cresol and other nitrophenol derivatives on respiration may conceivably be resolved into two factors. According to this view, one factor leads to stimulation, the other factor to limitation of the rate of oxygen consumption. The extent to which oxygen consumption can be made to rise above normal will then depend on the rate at which the stimulating and limiting factors change with respect to each other as the concentration of reagent is varied.

According to this hypothesis, dinitrothymol shows only a small stimulating effect because its ability to set a top limit to the extent of respiratory rise becomes evident at concentrations which might, if no limiting factor entered, lead to stimulation. That such a limiting factor may play a rôle is indicated by the representative data in Tables I and II.

Measurements of oxygen consumption and the extent of cell division were made with fertilized eggs of the sea urchin *(Arbacia punctulata)* using a technique described elsewhere.[1]

Table I shows that 10^{-6} molar dinitrothymol can entirely nullify

[1] Clowes, G. H. A., and Krahl, M. E., *J. Gen. Physiol.*, in press.

TABLE I.

Concentration 2,4-dinitrothymol moles per liter	Concentration 4,6-dinitro-o-cresol moles per liter	Oxygen Consumption c.mm. 0_2 per 10 c.mm. eggs	Divisions per egg in 3 hours
0	0	2.76	4.00
0	10^{-6}	3.70	4.00
0	$5x10^{-6}$	8.25	1.86
0	10^{-5}	8.70	0.39
10^{-6}	0	2.44	1.80
10^{-6}	10^{-6}	2.60	1.49
10^{-6}	$5x10^{-6}$	2.50	0.14
10^{-6}	10^{-5}	2.65	0

TABLE II.

Concentration 2,4-dinitrothymol moles per liter	Concentration 4,6-dinitro-o-cresol moles per liter	Oxygen Consumption c.mm. 0_2 per 10 c.mm. eggs	Divisions per egg in 3 hr.
0	0	2.65	3.80
10^{-7}	0	2.72	3.80
$2x10^{-7}$	0	2.68	3.84
$4x10^{-7}$	0	2.76	3.82
$8x10^{-7}$	0	2.76	3.59
$1.6x10^{-6}$	0	2.18	0.84
0	$4x10^{-6}$	7.02	3.68
10^{-7}	$4x10^{-6}$	6.65	3.64
$2x10^{-7}$	$4x10^{-6}$	5.75	2.52
$4x10^{-7}$	$4x10^{-6}$	4.03	1.06
$8x10^{-7}$	$4x10^{-6}$	3.16	0
$1.6x10^{-6}$	$4x10^{-6}$	2.36	0

the stimulating effect of an equal, 5 times greater, or 10 times greater concentration of dinitrocresol.

Table II illustrates the effect of varying concentrations of dinitrothymol combined with a single concentration of dinitrocresol. With increasing dinitrothymol concentrations, which alone have little or no respiratory effect, the respiratory rate in the presence of the combined reagents falls from an elevated one, produced by dinitrocresol alone, to a point approximating the normal value. Beyond this level, a large increase in dinitrothymol concentration is required to produce any further significant decrease in respiratory rate.

The division suppressing effects of the two reagents are additive.