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Stimulation of Oxygen Consumption and Suppression of Cell Division by Dihalo and Trihalophenols.

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It is known that the oxygen consumption of fertilized sea urchin eggs *(Arbacia punctulata)* can be markedly stimulated by the addition of suitable concentrations of nitro and dinitrophenols.[1, 2] Stimulation of oxygen consumption in these cells can also be effected by certain oxidation-reduction indicators.[5, 6] In concentrations slightly greater than the optimum for respiration, certain nitrophenols block the cell division of fertilized Arbacia eggs. This division block is fully reversible since the eggs, when returned to sea water after a 3-hour exposure to concentrations many times the optimum for respiration, resume division and develop to swimming larvae.[1] In concentrations which are optimum for respiration, a number of oxidation-reduction indicators also inhibit cell division in fertilized Arbacia eggs, but the eggs so treated do not recover when they are returned to sea water.[5, 6]

Since the chemical and biological properties of the nitro compounds differ in almost every respect from those of the oxidation-reduction indicators,[5] it has been tentatively concluded that the nitro and dinitrophenols do not stimulate respiration or block cell division as a result of any possible oxidation or reduction which they may undergo in the cell. For the production of the respiratory-stimulating and division blocking effects, the unesterified phenolic OH group, accompanied by suitable substituents in the benzene ring, appears essential.[3]

The experiments presented here support this view since they show that, in fertilized eggs of Arbacia punctulata, oxygen consumption is stimulated and cell division is reversibly blocked by phenols containing no nitrogen and no substituent group capable of oxidation-reduction. These phenols contain, in addition to the OH group and the benzene ring, only chlorine, bromine, or iodine atoms. Phenols of this type are oxidized irreversibly at high positive potentials.[4]

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

4 Fieser, L. F., *J. Am. Chem. Soc.*, 1931, **52**, 5204.

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From preliminary experiments it appears that, in low concentrations, the monohalophenols do not stimulate oxygen consumption or reversibly block cell division; the 2,4-dihalophenols are very active in this respect; the 2,6-dihalophenols are inactive; the 2,4,5-trihalophenols are very active, while the 2,4,6-trihalophenols, in contrast to 2,4,6-trinitrophenol, stimulate oxygen consumption and block cell division at high dilution.[3]

Experiments were conducted according to methods described elsewhere.[3] Typical results are presented on a percentage basis in Table I. With each of the 3 reagents, the block to division was completely reversible, since all samples of eggs, after return to sea water, gave 90-100% development to top swimming larvae.

TABLE I.

Oxygen consumption and cell division of fertilized eggs of *Arbacia punctulata* in sea water containing various concentrations of 2,4-dichlorophenol (I), 2,4,5-trichlorophenol (II), and 2,4-dinitrophenol (III). Temperature 20° C. The values are expressed as percentages of the controls.

Concentration of reagent moles per liter.	I		II		III	
	O_2 Uptake	Division	O_2 Uptake	Division	O_2 Uptake	Division
None—Control	100	100	100	100	100	100
4x10-6	100	100	170	100	126	100
8x10-6	107	100	250	77	171	100
1.6x10-5	111	100	264	5	256	98
3.2x10-5	123	100	153	0	291	10
6.4x10-5	230	99	103	0	268	4
1.28x10-4	236	19	100	0	240	5
2.56x10-4	156	11	100	0	204	3
5.12x10-4	124	3	100	0	159	4

To ascertain the effects of dihalo and trihalophenols on mammals, preliminary experiments with a number of these compounds have been carried out in collaboration with Dr. K. K. Chen. After intravenous injection, 2,4-dichlorophenol did not increase the metabolic rate of rats or the body temperature of pigeons or dogs.