

THEORY OF CATALYTIC ACTIVITY OF THE KETENONES

In the case of the peroxide of formaldehyde (which may be viewed as a half 'Ketene') in the presence of water, the instability is so great that decomposition is about complete within from two to six hours. Attendant conditions determine the rate and the direction of the change and how much tautomeric change to formic acid goes on. It is during this decomposition that the hydrogen atoms are oxidized to water and the carbonyl group is liberated, two such groups uniting to form glyoxylide transiently before they join oxygen to form carbon dioxide. It is an auto-oxidation mechanism. In the decomposition, a migration of hydrogen electrons to oxygen takes place and then a union of oxygen with unsaturated carbon atoms follows. The union of Glyoxylide or malonide with oxygen and its decomposition to carbon dioxide involves two migrations of carbon electrons, one from inside the molecule to the oxygen atoms, and the other within the molecule as the valences split between the oxygen atoms added and join the carbon atoms to which the oxygen atoms are already joined. Both types of electronic migrations have their catalytic values. Very few molecules need be changed to supply the high dilutions used.

The efficiency of activation of the unsaturated groups of the fluorescent substance to unite with oxygen here encountered may be compared with the auto-oxidation of benzaldehyde, where first a peracid, benzoyl hydrogen peroxide is formed, (A) which reacts with further

benzaldehyde to form benzoic acid (B). Baekstroem found that both reactions are sensitive to light, the quantum sensitivity of (A) being of the order of 10^4 , while (B) was much smaller a yield of 17 molecules per quantum (32). Thus the reaction between benzaldehyde and oxygen is highly efficient in causing the activation of fresh aldehyde molecules to react with oxygen. The mechanism is, of course, not fully understood even though in the case of comparatively stable substances here cited the peracid was isolated as an intermediary in the process. Still the ultimate activity is a facilitation of the migration of electrons to oxygen from a system of atoms in a large number of molecules by the act having just taken place or just going on in one molecule, so the medium of the intermolecular spaces must play a part. This medium must therefore convey a sort of resonated radiation between similarly constructed atom groups, which induces electronic migrations in progress in one group to take place in others of similar structure. The phenomenon is exemplified also by experimental mitogenetic radiations and the greater rate of epithelialization of proximate points of a healing wound.

To demonstrate the direct annulment of carcinogenic activity of the highest order, mice were painted with benzene solutions of benzopyrene in concentrations of one to two hundred three times a week for a period of weeks. At chosen periods a dose of one of the peroxides studied or of a crudely prepared solution of glyoxylide was given subcutaneously or intraperitoneally, once in some instances and oftener in others. By comparing the incidence of tumors and cancers in the controls and in the treated animals, an idea of their efficacies is obtained. The peroxide of diformaldehyde shows

splendid activity. The peroxide of formic acid shows less efficiency. The peroxide of oxalic acid in unreported experiments showed no protection, while the peroxide of formaldehyde showed repeatable recoveries from well established cancer as well as prophylaxis. When sufficient time has passed to demonstrate the permanence of recovery these observations will be published. The first observation was made together with Professor Maisin (31) and others were done by Professor Maisin and members of his staff (32) (33).

Protective Action of Diformaldehyde Peroxide

The mice received applications of benzene solution; 1/200 benzopyrene three times each week. The peroxide was injected, 1cc. solution 1/20,000, on the 35th and 65th days.

Groups	Mice at start	Mice surviv- ing to first To cancer	147th day	Day of observa- tion	Relative percent		Absolute percent	
					Tu- mors	Can- cers	Tu- mors	Can- cers
CONTROLS								
1	40	28	21	147th day	53	48	55	48
INJECTED								
2	50	40	27	147th day	4	—	5	2.5

Peroxide of Diformaldehyde

1/20th of a mgm as one dose was given at the end of the first month of benzopyrene application.

Groups	Mice surviving to first cancer	To	Percentage absolute of cancer
Controls	28	120th day	18
		210th day	57
Injected	40	120th day	5
		210th day	7.5

1/10 mgm of the peroxide of diformaldehyde was given as one dose intraperitoneally before the first benzopyrene application.

Controls	78	120th day	30
Injected	75	120th day	10

Mice receiving three drops a week for 6 to 7 weeks of a benzene solution of benzopyrene, of a strength of one to two hundred. For treatment each animal received one dose of $\frac{1}{2}$ cc. of a 1/5000 solution of the peroxide of formic acid.

Groups	Mice surviving to first cancer	To	Percentage absolute of cancer
Controls	68	120th day	45
		210th day	69
Injected	52	120th day	23
		210th day	31

For treatment each mouse received 1/10 mgm as one dose of diformaldehyde peroxide every 14 days after the first application of benzopyrene.

Controls	78	120th day	30
Injected	30	120th day	9

Unsaturated Substances

All mice received twenty applications of a benzene solution of benzopyrene 1/200 three times a week for twenty doses, and then one dose of an alkaline solu-

tion of 0.10 mgm of a fraction of the distillate obtained by the action of strong sulphuric acid upon ethyl ether. This distillate crudely contains, among other things, the sulphurous acid compounds of the diketal, glyoxylide, and related bodies.

EXPERIMENT A

		<i>Controls</i>			<i>Injected</i>		
		Number of mice alive	Percent of tumors	Percent of cancer	Number of mice alive	Percent of tumors	Percent of cancer
Day	60	75	36	1	62	10	0
Day	80	72	50	8	61	30	1.5
Day	100	71	65	16	60	38	4
Day	120	66	67	22	56	38	10

EXPERIMENT B

Day 60	60	71	28	0	75	22	0
Day 70	70	70	40	5	69	27	1

Thus the injected animals demonstrate destruction of the allergenic activity of benzopyrene; both by the unsaturated diketones which may become peroxides within, as well as outside the body, and by the peroxides of substances which in the body may liberate free carbonyl groups to form the unsaturated diketone and also catalyze the peroxidation of formaldehyde. So, in a laboratory way we here hint at their therapeutic value which we have proven nearly twenty years ago by the full cure of human beings suffering with far advanced fully diagnosed cancer; cases that were too far advanced for operation, or were operated by experts with widespread recurrence and extension of the disease resulting.