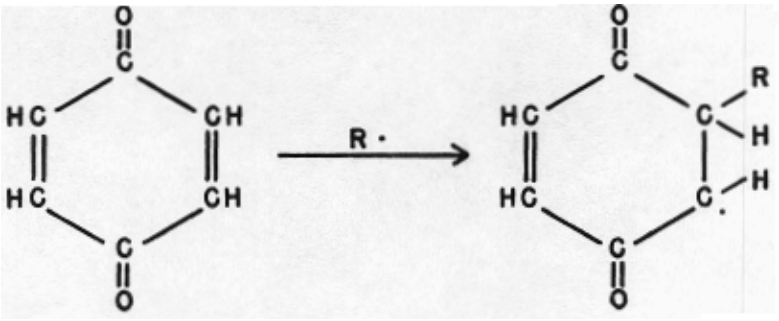
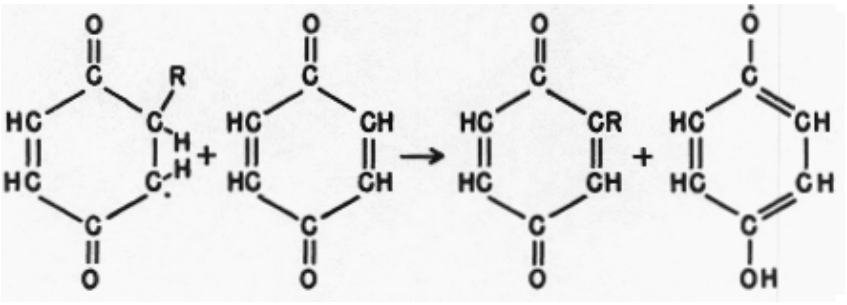
CHAPTER 10

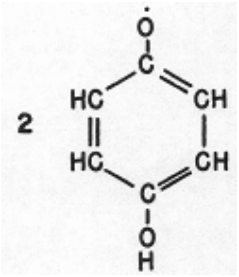
RECENT PHARMACEUTICAL STRIDES

Very recently, in the last few years, some highly substituted Benzoquinones have been introduced into medicine, as cytolytic agents in the treatment of cancer. The high substitution defeats any action, inherent to the quinone structure that might be curative. Such action depends upon high activation of the Carbonyl group, and upon the wealth of resonance hybrids that would be possible if the hydrogen atoms, held by the ethylene linkage were present, instead of displaced by complex groups that not only prevent electron migrations to the Carbonyl group, but prevent additions of free radicals to the carbon atoms of the ethylene groups. In certain instances, the benefit of Benzoquinone is due to its ability to absorb antagonistic free radicals, and the high substitutions annul this effect. The following well recognized reactions might be offered as a demonstration of this detoxicating quality, which is lost in the admitted non-curative commercial drugs.

(Well-established free radical absorbing power of Benzoquinone...)



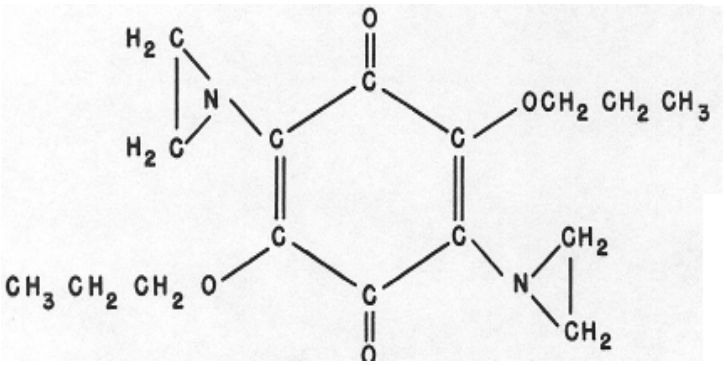




…yields the Quinhydrone, which is disproportionate to Hydroquinone and Benzoquinone. Thus, Benzoquinone inactivates free radicals and the therapeutic action is hindered, as clinical tests have proven. We therefore conclude, that the therapeutic activity of these Reagents is partly, at least, to be attributed to the free radicals they contained and which, were responsible for the oxidation and polymerizations in progress in these systems. There is nothing cytolytic about this structure. It is constructive in action.

Pharmaceutical Substituted Quinones

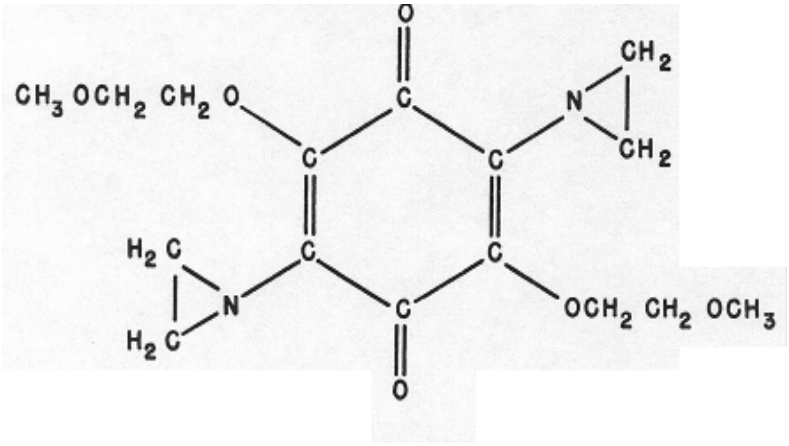
As examples of these cytolytic agents that are admittedly unable to protect or to cure, the following of Schenley Laboratory may be taken as an example:



It carries toxic nitrogen, -2,5 -di-n propxy-3,6-bis-ethylenimine- 1 ,4 Benzoquinone.
And the following A-139 is of the same order:

Actinomycin is a natural nitrogen free antibiotic that has had some trial but without any curative results. Whatever they are, they might be a little better than that of the preceding or Bayer's E39, which is built on the same order as Schenley's and A-139. In Actinomycin, Carbonyl activity is limited by the substituents, and by the failure to have

even one hydrogen atom attached to an ethylene linkage. This again is for the benefit of the organism that produces it and not to serve as a therapeutic agent.



Certainly, the analytical and synthetic work of the antibiotic chemist deserves the highest praise. The search for virtue in complexity of structure, however, has no basis aside from the needs of the organism that produces the antibiotic. These are not identical with the requirements of higher animals in the situations we have discussed. Rather the greatest simplicity possible wins the laurels here.