

Chemical and electrical gradients exist across the cell membrane and these represent a proton-motive force which drives such essential processes as oxidative phosphorylation, adenosine triphosphate (ATP) synthesis and active transport; several agents act by reducing the proton-motive force. The cytoplasm, which is the site of genetic control and protein synthesis, presents a target for those chemical agents that disrupt ribosomes, react with nucleic acids or generally coagulate protoplasm.

Principal factors affecting activity

The factors most easily quantified are temperature and concentration. In general, an increase in temperature increases the rate of kill for a given concentration of agent and inoculum size. The commonly used nomenclature is Q_{10} (temperature coefficient), which is the change in activity of the agent per 10 °C rise in temperature (e.g. Q_{10} phenol = 4).

The effect of change in concentration of a chemical agent upon the rate of kill can be expressed as:

$$\eta = \frac{\log t_2 - \log t_1}{\log C_1 - \log C_2} \quad (15.4)$$

where C_1 and C_2 represent the concentrations of agent required to kill a standard inoculum in times t_1 and t_2 . The concentration exponent η represents the slope of the line when log death time (t) is plotted against log concentration (C).

When values of η are greater than 1, changes of concentration will have a pronounced effect. Thus, in the case of phenol, when $\eta = 6$, halving the concentration will decrease its activity by a factor of 2^6 (i.e. 64-fold), whereas for a mercurial compound, $\eta = 1$, the same dilution would only reduce activity twofold (2^1). Further details and tabulations of both temperature coefficients and concentration exponents may be found in Denyer & Wallhaeusser (1990).

Range of chemical agents

The broad categories of antibacterial chemical compounds have remained surprisingly constant over the years, with phenolics and hypochlorites comprising the major disinfectants and quaternary ammonium compounds widely used as antiseptics. The compounds capable of use as preservatives in

preparations for oral, parenteral or ophthalmic administration are obviously strictly limited by toxicity requirements. As concerns over toxicity have intensified, the range of available preservatives has diminished: mercury-containing compounds, for example, are now very little used for the preservation of parenteral and ophthalmic products. The high cost of research and testing coupled with the poor prospects for an adequate financial return militate against the introduction of new agents. For this reason there is a tendency towards the use of existing preservatives in combination, with a view to achieving one or more of the following benefits: synergy, a broader antimicrobial spectrum or reduced human toxicity resulting from the use of lower concentrations. The subjects of preservative toxicity and their potentiation and synergy are reviewed by Denyer & Wallhaeusser (1990), and Moore & Payne (2004) have described in detail characteristics of the commonly used biocides. Table 15.3 summarizes the properties and uses of the major groups of biocides.

Phenolics

A limited selection of phenolic compounds is shown in Figure 15.4.

Various distillation fractions of coal tar yield phenolic compounds, including cresols, xylenols and phenol itself, all of which are toxic and caustic to skin and tissues. Disinfectant formulations traditionally described as 'black fluids' and 'white fluids' are prepared from higher-boiling coal tar fractions. The former make use of soaps to solubilize the tar fractions in the form of stable homogeneous solutions, whereas the latter are emulsions of the tar products and unstable on dilution.

Remarkable success has been achieved in modifying the phenol molecule by the introduction of chlorine and methyl groups, as in chlorocresol and chloroxylenol. This has the dual effect of eliminating toxic and corrosive properties while at the same time enhancing and prolonging antimicrobial activity. Thus, chlorocresol is used as a bactericide in injections and to preserve oil-in-water creams, whereas chloroxylenol is employed as a household and hospital antiseptic. Phenol may itself be rendered less caustic by dilution to 1% w/v or less for lotions and gargles, or by dissolving in glycerol for use as ear drops. Bisphenols, such as hexachlorophane and triclosan (Irgasan), share the low solubility and enhanced activity of the other phenol