

conclude that, because this hormone is normally synthesised by the animal and enters a well-known biochemical pathway, the extra dose probably enters the same biochemical pathway and modulates the aging process but, unfortunately, most tested molecules are not copies of those naturally produced by the organism. By contrast, let us imagine that an experimenter shows that a low dose of the highly toxic molecule Y has positive effects on lifespan and aging: one could conclude that its mechanism of action is probably hormetic but, unfortunately again, most tested molecules are not highly toxic.

Nevertheless, many drugs have hormetic effects even when they are not highly toxic. Some drugs are beneficial at low doses and toxic at high doses, like for instance paracetamol or aspirin. Other drugs have deleterious effects at low doses and beneficial ones at high doses, like antibiotics that stimulate growth of bacteria at low doses and kill them at high doses or anti-tumour drugs.⁵³ In both cases, these drugs display a hormetic dose-response curve, with opposite effects at low and high doses, and the physician relies on symmetrical strategies to treat the disease: low doses of paracetamol against pain and fever, and high doses of antibiotics to kill bacteria (Figure 3.3).

However, even if one is able to discover a molecule with positive effects on lifespan and health at old age in animal models, an issue is that this molecule could have an effect only in short-lived (see above) or compromised animals (see below) and thus would not be a real “anti-aging” drug, even if useful in therapy.

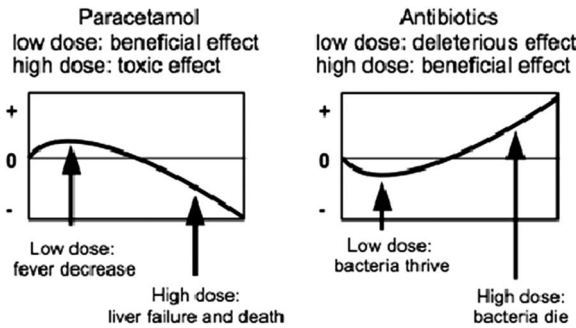


Figure 3.3 Hormetic dose-response curves showing opposite effects at low and high doses. The ordinates show beneficial (+), neutral (0), or deleterious (-) effects for the patient. Different drugs can have either beneficial or deleterious effects at a low dose and two examples are shown. Low doses of paracetamol decrease fever or pain, but very high doses can lead to death because of hepatotoxicity. Low doses of antibiotics can stimulate bacterial growth because they disturb the homeostasis of the bacteria without inducing severe damages and provoke a general adaptive response, enhancing the ability of bacteria to proliferate. By contrast, high doses are toxic to bacteria and kill them, which is the expected therapeutic effect of antibiotics.⁵³