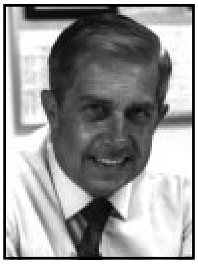

Fact or Fiction?

Jack W. Dini
1537 DeSoto Way
Livermore, CA 94550
E-mail: jdini@earthlink.net

Hormesis: A Little Bit Is Good—Too Much Is Bad

Did your mother ever tell you that a little bit of something was good for you but too much would make you sick? A case in point is my experience with chocolate, which I've always loved. I was helping my uncle who owned a bakery and my job one day was to clean five-gallon cans of chocolate. As part of my cleaning process, I sampled too much of the chocolate left on the insides of the cans. I got very sick—a case of too much of a good thing. This is an example of hormesis which is a fancy sounding name that means high doses and low doses produce opposite effects with low doses providing beneficial effects and high doses the opposite. Hormesis applies throughout nature. There are many hundreds of studies in the literature that describe experiments and observations supporting the beneficial effects of chemical and physical agents at low doses.[1] Hormesis also applies to radiation, but this will be covered in a future column.

The word "hormesis" derives from the same root as hormone, from the Greek *hormo*, "I excite." Although the word is new, the concept is quite old, having been described by Hippocrates and others.[2] They were all concerned with dose. They recognized that the dose was everything and stress was the common denominator. Small stresses stimulated, while excess stresses inhibited.

Hormology, the study of excitation, includes physical, chemical and biologic cases. One example is the melting point of a mixture of two metals. Addition of one to the other lowers the melting point until the eutectic point is reached; then adding more of the same metal to the mixture increases the melting point. Electroless nickel and tin-lead deposits are two coatings which exhibit this phenomenon.

Chemical hormesis is well known in catalysis. Biochemistry examples include enzymes and their activation. Under proper conditions, enzymes can increase reaction rates a thousand times, but an excess of the same material decreases the reaction rate.[2] Tetrodotoxin is an interesting biologic example. This material, which is 100,000 times more toxic than plutonium, is a natural hallucinogen found in the Fugu, the puffer fish treasured for centuries in Japan. As Luckey[2] points out: "A small amount of tetrodotoxin produces euphoria; too much produces severe paralysis. In fact, overdoses are thought to kill dozens of Japanese each year. It is also the principle ingredient of the mixture used in creating zombies by Haiti witch doctors."

Hormesis has been observed in bacteria, fungi and yeasts, plants, algae, invertebrates and vertebrates, and in cell cultures.[3] The agents used in these studies included metals, such as cadmium and lead, solvents and many synthetic and natural chemicals. Polychlorinated biphenyls (PCBs) were shown to promote the growth of juvenile Coho Salmon and minnows. The growth of clam and oyster larvae was promoted by low level concentrations of some 52 pesticides, and chlordane and lindane have been shown to promote the growth of crickets.

In terms of animals, chemically induced hormetic effects have been claimed for crabs, clams, oysters, fish, insects, worms, mice, rats, ants, pigs, dogs and humans. The range of agents employed in such studies has been wide, including numerous antibiotics, PCBs, ethanol, polycyclic aromatic hydrocarbons (PAHs), heavy metals, essential trace elements, pesticides and a variety of miscellaneous agents, including chemotherapeutic agents, solvents such as carbon tetrachloride, chloroform, cyanide, sodium and others.[4] A 1994 publication by the American Industrial Health Council listed 30 studies showing beneficial effects for lead, nicotine, PCBs, toluene, alcohol, jet fuel, methyl mercury and several other poisons.[5]

Absolute purity is out of the question with productive waters. Kazmann[6] reports, "If the Mississippi river passing between Baton Rouge and New Orleans consisted of distilled water there would be no seafood industry such as we now have in Louisiana. Without copper contamination in the water there would be no oysters. Traces of iron, manganese, cobalt, copper and zinc are essential for crabs, snapper, flounder, shrimp and other creatures that abound in Gulf waters."

The use of vitamins as daily dietary supplements based on their beneficial effects at low doses is an example of hormesis. Overdose of the more fat soluble vitamins such as A, E, and D have toxicities associated with them.[7] Water soluble vitamin B6 can cause nerve damage at high doses. Hormones such as estrogen can cause cancer.[8] If you breathe pure oxygen at normal room pressure, you will suffer chest pain, coughing and a sore throat within six hours. Hospitals have found that premature babies placed in incubators that were filled with oxygen enriched air went blind because of oxygen damage to their retinas.[9] Even water itself can be fatal if the rate of intake exceeds the body's capacity to process it (and I'm not talking about drowning, rather drinking too much water). In Germany, a man died from cerebral edema and electrolyte disturbance because he drank 17 liters of water within a very short time.[10] Overuse of ethanol is associated with numerous organ toxicities but these days you can read many claims about reduced risk of coronary heart disease, reduced mortality, etc., from moderate consumption of alcohol.

At the end of the 19th century, only two elements (iodine and iron) were known to be essential for human health. By 1935, only four more (copper, manganese, zinc and cobalt) had been added. Progress has been more rapid during the past 40 years (see table), largely because the revolution in analytical chemistry has greatly enhanced the experimenter's capability to measure trace elements in the extremely small quantities present in plant and animal tissues and in food.[11] The main reason for the extraordinary potency of essential trace elements is that most of their work is done as components of enzymes or hormones. Note that lead and cadmium are included in the accompanying table. Heiby,[12] in his tome, *The Reverse Effect*, containing 1216 pages and 4821 references, lists a number of examples where extremely minute amounts of these metals may be important to the human body.

Practically every enzyme in the body has some small amount of metal involved in its chemical structure. Zinc is used to maintain cell membranes and produce protein and energy; either too much or too little can lead to reduced growth. Iron and molybdenum also must be kept at moderate levels.[8] Excess iron leads to hemochromatosis, where massive amounts of iron, as ferritin and hemosiderin, are laid down in the body tissues.[13] Other cases of iron overload are specific anemias, where excessive breakdown of blood occurs, liver disease and massive blood transfusion. Copper is essential in minute quantities to the normal functioning of the human body. It makes possible the assimilation of iron, but like some other members of this company (most notably iron), its impact in large quantities has long been known to be toxic. Wilson's disease is essentially chronic copper poisoning. In it, the natural balance between copper ingestion and copper excretion is disturbed and the copper retained is stored in certain organs. Symptoms of the disease include a sweeping range of neurological disturbances—slurred speech, failing voice, excessive salivation, drooling, difficulty in swallowing, tremors, coordination difficulties, spasticity and muscular rigidity.

Essential Trace Elements
In the Human Body*

Element	Date of recognition of essential role
Iron	17th century
Iodine	19th century
Copper	1928
Manganese	1931
Zinc	1934
Cobalt	1935
Molybdenum	1953
Selenium	1957
Chromium	1959
Tin	1970
Vanadium	1971
Fluorine	1971
Silicon	1972
Nickel	1974
Arsenic	1975
Cadmium	**1977
Lead	**1977

*From Lenihan, ref. 11.
**Evidence incomplete, but see Heiby, ref. 12.

As *Runner's World* reported: "Chromium is not just for bumpers anymore."[14] The article claims that chromium assists the hormone insulin, which is vital for proper glucose control and for protein production in muscles. Other claims are that chromium supplements promise to be new treatments for heart disease, high blood cholesterol and diabetes.[15] The metal even has its own book, *The Chromium Caper*, by J. Fischer. As Fumento[16] discloses; "It's another one of those diet books that could be summed up in a single sentence: Make sure you get enough chromium in your diet." Excessive doses of chromium may suppress growth but only with quantities far in excess of those encountered in the food and supplements containing yeast or amino-acid chelates.[13]

Selenium, once thought to be a poison and a carcinogen, has been found to be an anti-tumor agent in relatively low doses and an essential nutrient with a very small difference between recommended and harmful doses.[2] Arsenic compounds, which are known human carcinogens, have been shown to widely stimulate the growth of chickens, calves and pigs. Some chlorinated dioxins and furans, widely considered as carcinogens, have been patented as anti-tumor agents.[3] Recently, arsenic trioxide has been used successfully in intravenous form for the treatment of acute promyelocytic leukemia in humans.[17,18]

The above information is not meant to be all-inclusive and the beneficial claims can change based on new research. Stewart[19] jokingly scoffs that as one scientist announces that some food is bad for you, five other scientists will release findings proving that the food only is bad for you if you are a 185-pound, middle-aged laboratory rat. He said there have been so many contradictory reports from scientists about cholesterol that three years ago his wife gave up eating entirely. All kidding aside, the point to be made is that there is enough evidence to support the fact that many chemicals and metals that are clearly toxic at certain dose levels offer beneficial effects at low doses.

What's the Point?

The important issue is that most of the time we receive only the bad news. The entire regulatory orientation is to look for an adverse effect, not a hormetic one. The designs of most toxicology studies emphasize almost exclusively the upper end of any possible dose-response curve. For example, research on most agents begins with the determination of LD-50 values (the dose of a chemical that will kill 50 percent of the test animals).[4] As McKenna[7] points out, "In the face of spiraling costs for remediation of environmental risks by both government and private sectors, the potential for greater accuracy in depicting chemical risks offered by consideration of hormetic effects seems a major benefit." Approaches traditionally used by the EPA have not incorporated deviations from linearity, nor have they tended to examine data (low-dose or other) that do not show a correlation of dose with some adverse effect. Remember this when you hear about the next environmental scare of the month. Ask the question: Instead of an animal consuming 50,000 to 100,000 times what a human would, what are the effects of low doses? They could be beneficial. P&SF

References

1. W.H. Baarschers, *Eco-Facts & Eco-Fiction*, Routledge (1996).
2. T.D. Luckey, *Radiation Hormesis*, CRC Press (1991).
3. A.R.D. Stebbing, *Science of the Total Environment*, **22**, 213 (1982).
4. E.J. Calabrese, M. E. McCarthy & E. Kenyon, *Health Physics*, **52**, 531 (1987).
5. E.J. Calabrese, "Biological Effects of Low Level Exposures," *AIHC Journal*, pp. 7-15 (Spring 1994).
6. R.G. Kazmann, "Environmental Tyranny-A Threat to Democracy" in *Rational Readings on Environmental Concerns*, J. H. Lehr, Ed., Van Nostran Reinhold (1992).
7. E.A. McKenna, *Int. J. Environment and Pollution*, **9**, 90 (1998)
8. A. Wildavsky, *Searching for Safety*, Transactions Books (1988).
9. B. Bova, *Immortality*, "How Science is Extending Your Lifespan & Changing the World," Avon Books (1998).
10. E. Efron, *The Apocalyptics: Cancer and the Big Lie*, Simon & Schuster (1984).
11. J. Lenihan, *The Crumbs of Creation*, Adam Hilger (1988).
12. W.A. Heiby, *The Reverse Effect*; "How Vitamins and Minerals Promote Health and Cause Disease," MediScience Publishers (1988).
13. L. Mervyn, *Minerals and Your Health*, Keats Publishing (1984).
14. A. Bean, *Runner's World*, p. 24 (Feb. 1994).
15. *San Francisco Chronicle* (May 18, 1989).
16. M. Fumento, *The Fat of the Land*, Viking (1997).
17. S.L. Soignet, P. Maslak, Z.-G. Wang, *et al.*, *New England J. of Medicine*, **339**, 1341 (1998).
18. R.E. Gallagher, *New England J. of Medicine*, **339**, 1389 (1998).
19. D.L. Stewart, "When It Comes to Science, Trust But Verify," *San Francisco Chronicle* (April 15, 1998).