Endorphins: New types and sweet links

Humans have known the analgesic effects of opiates for centuries, but it was not until the early 1970s that scientists discovered opiates work by attaching to specific receptor cells in the nervous system. Unable to believe that opiate receptors evolved in the brains of higher animals in order to react with a product of the opium poppy, scientists reasoned that the body produces endogenous morphine-like substances, or endorphins.

In 1975, researchers isolated the first endorphins from nervous tissue, and the race to find out how and why animals make opiates was on. Now, one group of researchers has found a new type of endogenous opiate by using antibodies to morphine, while another group has discovered that specific sweet substances may activate the endorphin system.

All endorphins characterized so far are peptides, long chains of amino acids. Chemically, peptides look nothing like morphine, a multi-ringed, nitrogen-containing base known as an alkaloid. But physiologically and behaviorally, the two act alike. Both bind to the same receptor cells and both are powerful analgesics, blocking the reception of pain without reducing other sensations.

In order to study opiate reception more closely, Sydney Spector and colleagues at the Roche Institute of Molecular Biology in Nutley, N.J., developed monoclonal antibodies (SN: 5/7/83, p. 296) to morphine. While the antibodies bind heartily to morphine, they fail to bind the peptide endorphins. "We don't know if the antibodies bind to morphine in the same way a brain receptor does," says Spector, who described his findings at the annual meeting of the American Society for Pharmacology and Experimental Therapeutics earlier this month. "But we do know the antibodies are much more specific."

Though the antibody does not bind to peptide endorphins, it does bind to at least three chemicals in extracts of beef brain. When Spector tested these chemicals' ability to compete with labelled morphine for opiate receptor cells, he found that "at least one of the three has twice the affinity of morphine" for binding sites. The extract also competed "very successfully" with morphine for binding sights on the morphine antibodies.

The group doesn't yet know what the new opiates look like, or if they are chemically similar to morphine. According to a common theory, alkaloids such as morphine provide chemical protection to plants, discouraging animal attacks. "The brain doesn't produce any alkaloids that we know of," says Spector. "But if plants can make them, why can't we?"

The extracts' function also remains a mystery. "It's classified as an opioid based on the fact that it binds to morphine receptors," Spector says. "We don't know if it has analgesic effects." Researchers have identified specific endogenous ligands — agents that bind to receptors—for some of the brain receptor sites. But, according to Spector, at least one receptor site lacks an identified endogenous ligand. "We hope the extract might play this role," he says. "But so far, we have no evidence."

The main obstacle Spector faces in gathering such evidence lies in the dearth of the new opioids. The brain produces such minute amounts — much smaller than originally thought—that researchers have a hard time accumulating enough of the opioids to characterize them.

Meanwhile, a group of scientists at Hebrew University in Jerusalem have been examining the connection between sweets and endorphins. Previous studies show that endorphins aid in the metabolism of sweet substances. In the Aug. 26 SCIENCE, the group reports that the reverse may also be true—sweets may cause the body to release its natural opiates.

In a behavioral study, Elliot M. Blass, now of Johns Hopkins University in Baltimore, and colleagues compared average rats with those bred for their propensity to drink saccharin. After feeding rats either water or saccharin, Blass tested their perception of pain by measuring the time each animal took to respond to being on a hot plate.

The researchers then gave the rats morphine, and repeated the test at 15-minute intervals. Rats who drank relatively little or no saccharin tolerated the hot plate longer at successive tests, theoretically because the morphine reduced the animal's perception of pain.

But morphine did not seem to affect the rats who drank a lot of saccharin, as they did not increase their latency time. "Though we don't know the neurophysiological basis of this," says Blass, "behaviorally, our study shows that rats who drink excessive amounts of saccharin build up a tolerance to morphine." He suggests that saccharin may induce endogenous opiates, which in turn may block morphine analgesia by occupying receptor sites in the nervous system.

Blass stresses that the team used a very specific genetic line of rats that drank the human equivalent of 3 to 4 gallons of highly concentrated saccharine solution every day for almost a month. "Until these findings are tested further," he says, "we don't know if they hold for other animals."

Will the findings hold for non-saccharine sweets, such as sugar? "My guess is probably," says Blass, who feels the answer will be known within the year. That answer could elucidate the link between the pleasurable perception of "sweet," the body's natural opiates and the proverbial sweet tooth. Researchers don't yet know if sweet substances actually activate the opiate system, or if it is because the system is activated that we perceive them as sweet. —*S. Steinberg*

Paraquat for U.S. marijuana sanctioned

Using the herbicide Paraquat to eradicate marijuana crops grown illicitly on federal lands will have "no significant effects upon the environment," according to an environmental assessment report just published by the U.S. Drug Enforcement Administration (DEA), an agency of the Department of Justice. The report also states DEA's intention to "undertake in 1983 to encourage the use of Paraquat spraying ... where appropriate, safe, feasible, and effective" as part of its multi-fronted assault on the illegal use of marijuana in this country. And in apparent consistency with that intention, the DEA last week directed the spraying of Paraquat on some 60 marijuana plants in sections of the Chattahoochee National Forest in northern Georgia, and on about 80 plants—some as tall as 18 feet—in Kentucky's Daniel Boone National Forest.

In its report, the DEA provides "guidelines governing all aspects of the criteria for target selection, Paraquat formulation and application, spray drift control, and safety procedures." Much of its content is based on that of an environmental impact statement published in 1979 by the U.S. State Department's Bureau for International Narcotics Matters, which assessed the past use of Paraquat spraying in Mexico. Critics, however, including Ellen Silbergeld of the Environmental Defense Fund, are skeptical that a study of Mexico's experience with the toxic herbicide is applicable to the United States. Typically, marijuana in Mexico is grown in large open fields, Silbergeld told SCIENCE NEWS, whereas in the United States it is grown in small patches. She maintains that attempting to spray these patches from the air requires such pinpoint accuracy that it is inevitable that Paraquat will end up on more than just marijuana. □

Bureau of Narcotics and Dangerous Drugs

Marijuana leaves