Novel buckyball blocks AIDS virus enzyme

In a strange twist of fate, scientists have found a particular type of buckyball – one of the family of all-carbon molecules called fullerenes – that inhibits the growth of HIV, the AIDS-causing virus.

Raymond F. Schinazi, a viral pharmacologist at the Emory University School of Medicine in Atlanta, and his colleagues report that a buckyball specially tailored to fit into the active site of a key HIV enzyme – HIV protease – paralyzes the virus, rendering it noninfectious in human cells grown in the laboratory. The fullerene is also toxic to the virus itself but does not appear to harm host cells. The team's report appears in the August JOURNAL OF ANTIMICROBIAL AGENTS AND CHEMOTHERAPY.

While the scientists stress that this new compound is not a treatment for AIDS, they do maintain that the new results could lead to future compounds that might have medicinal value.

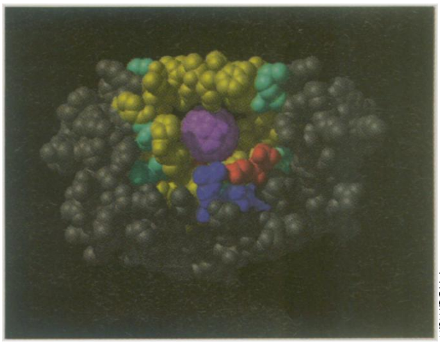
"This is not a drug for AIDS," says Schinazi. "But it appears to be the first practical biological application of buckyballs."

Schinazi and his colleagues report that the uniquely shaped, water-soluble "fulleroid" disarms the HIV virus and blocks HIV protease from cutting proteins, without damaging the infected cells themselves. The fulleroid showed antiviral activity in three types of cultured human immune cells infected with HIV. It also acted on the virus' reverse transcriptase, and thus inhibited HIV's ability to infect cells.

Restraining the researchers' enthusiasm, though, is the fulleroid's low potency, compared with AZT and other HIV enzyme-inhibiting drugs. To be useful as a drug, the fulleroid must be "at least 1,000 times more potent," says George L. Kenyon, a pharmaceutical chemist at the University of California, San Francisco, who aided in the fulleroid's development.

"I would say these fullerenes represent a potentially interesting new lead," says Craig L. Hill, a chemist at Emory University who coauthored the report. "At the present time, however, the collective knowledge from the little research to date is insufficient to get truly excited [about]. Very little is known about the tolerance of these compounds in mammals."

The fulleroids that Schinazi used were the brainchild of Simon H. Friedman, a graduate student working in Kenyon's lab. While Friedman was searching for compounds to block HIV protease, a colleague jokingly asked, "What next, buckyballs?" Friedman didn't laugh. Instead, he called up a model of an HIV protease on his computer and saw that a buckyball would fit perfectly into the protease's active binding site – if only the fullerene would dissolve in water.



Friedman

A model of the HIV-1 protease, with a buckyball (purple) binding to the active site, thus blocking protein cutting.

Friedman sought the help of Fred Wudl, a fullerene expert at the University of California, Santa Barbara, who fashioned a water-soluble version with two charged arms to grasp the protease's binding site. In lab tests, the fulleroid did in fact fill the protease's cavity, thus inactivating it.

Friedman and his colleagues present their results in the July 28 JOURNAL OF THE AMERICAN CHEMICAL SOCIETY, along with a separate report by Rint Sijbesma, a chemist at the University of California, Santa Barbara, and co-workers detailing how to make water-soluble fulleroids. – *R. Lipkin*

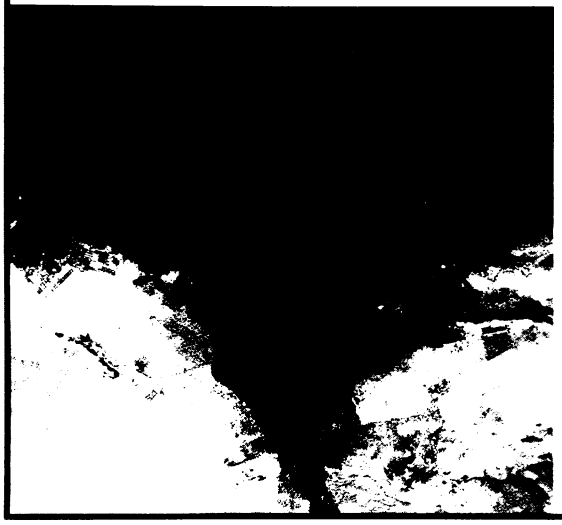
Pottery shows Nile delta dropping fast

Ancient pottery fragments discovered by chance near the mouth of the Nile reveal that parts of this agriculturally important delta are sinking substantially faster than scientists had thought, a finding that bodes ill for the future of Egypt's breadbasket.

The delta is dropping in part because the massive load of sediment laid at the mouth of the Nile causes Earth's crust to sag there. Called subsidence, this process occurs at most major river deltas. Natural floods normally rebuild the sinking land surface by depositing new sediment, but the Nile's Aswan dams have stopped the annual floods and shut off the source of replenishing silt.

To gauge the rate of subsidence across the Nile delta, Daniel Jean Stanley of the Smithsonian Institution in Washington, D.C., and Andrew G. Warne of the U.S. Army Corps of Engineers in Vicksburg, Miss., have drilled 100 holes in the region, collecting cores of the layered sediments deposited on the delta. Because the layers record where sea level was millennia ago, the researchers can determine the speed of subsidence by dating the sediments. In the April 30 SCIENCE, Stanley and Warne reported that carbon-14 dating technique suggested that various parts of the delta were sinking 1 to 5 centimeters per decade.

That now appears an underestimate, according to archaeological dating of potsherds preserved within one of the cores. The shards date to various periods of Egyptian history from 3,600 to 2,000 years ago. In all cases, the shards appear significantly younger than the carbon-14-dated sediment layers in which they were found, Warne and Stanley report in the August GEOLOGY.



Earth Satellite Corp./SCIENCE

Vegetation on the Nile delta shows up red in this mosaic of Landsat images.

For various reasons, researchers regard dates obtained through archaeological methods as more reliable than those determined by the carbon-14 method. In some of the Nile cores, the carbon-14 dates record the much greater age of organic matter preserved in the younger sedimentary layers.

The revision in dates suggests that the site where the shards were preserved is sinking more than 1½ times faster than previously estimated. The authors suggest that calculated subsidence rates at other sites are also too low. The effects of subsidence combine with those of rising sea levels, which are currently climbing 1 centimeter per decade and could accelerate in the future.

The combined effects of subsidence and sea-level rise create erosion along the coast and threaten to inundate some delta areas in the next century, Stanley says. Even more important, he adds, the amount of arable land will shrink as saline groundwater seeps southward and salts accumulate in the surface soils. – *R. Monastersky*