Deadly poison may hold key to cancer drug

By DAVE GUILFORD
Village News

Just as penicillin was hailed as the "miracle" drug of the 20th century, nature may again yield a major breakthrough, this time in the race to treat cancer. An unassuming mushroom often found in Balboa Park could be the biochemical basis of a treatment for pancreatic, ovarian and prostate cancers.

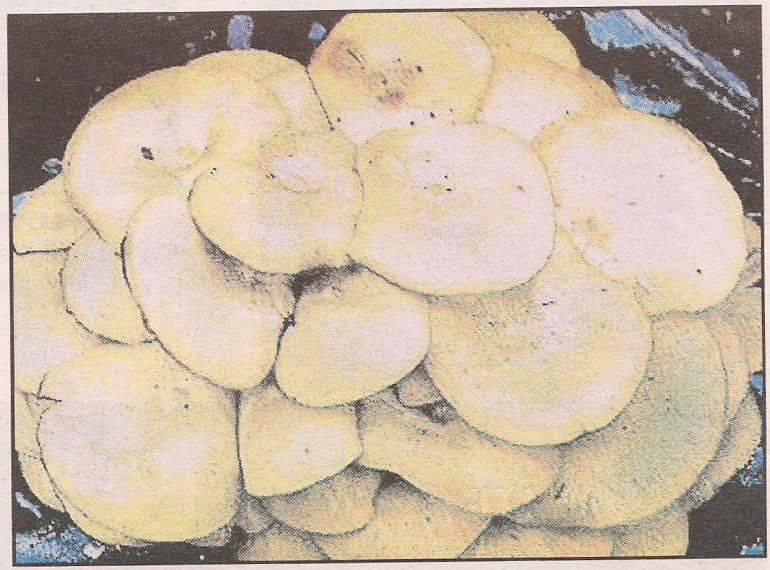
Two scientists at the University of California, San Diego (UCSD) and a Minnesota pharmaceutical company are betting on it. Dr. Trevor McMorris, a professor of chemistry and biochemistry at UCSD, began studying the chemical makeup of the jack o' lantern mushroom in 1960. It was determined that these orange-and-yellow-colored mushrooms, though highly toxic, contained illudin-S, a viable anti-tumor agent. McMorris set about determining the nature of illudin-S in late 1960.

"I was lucky, in that we were able to figure out the chemical structures of illudins in a couple of years," McMorris said. "In fact, we published our first paper in 1963 on the structures of the illudins."

Once the chemical structure of illudin had been discovered, McMorris began synthesizing compounds based on illudin, with two major objectives. These compounds, called acylfulvenes, had to be more effective at shrinking malignant tumors, and less toxic to the patient.

Dr. Michael Kelner, professor of

see Cancer drug, page 4



UCSD researchers are studying the anti-tumor properties of orange and yellow jack o' lantern mushrooms.

Cancer drug
from page 1

pathology at the UCSD School of Medicine, began testing these acylfulvenes in the late 1980s. Special "nude" mice (mice with no immune system) are used in the testing. They are injected with cancer cells, and once a tumor develops, the acylfulvene compound is introduced. Some of the compounds worked better than others.

Once Kelner found the most promising compound, he and Dr. McMorris applied for patent protection through the university. This compound is now called irofulven.

MGI-Pharma (Nasdaq: MOGN), a pharmaceutical company based in Bloomington, Minn., acquired the rights to irofulven (and all other illudin-S analog compounds developed by McMorris and Kelner) from the University of California in 1993.

According to MGI-Pharma's 1999 Annual Report, "Irofulven has demonstrated complete shrinkage of more than 10 different types of human solid tumors transplanted into mice, including pancreatic, prostate, ovarian, breast, lung and colon tumors. Human studies have been initiated to confirm irofulven's broad spectrum of anti-cancer activity. In each of three initial MGI-sponsored Phase 2 studies of prostate, pancreatic and ovarian cancer, objective anti-cancer responses have been demonstrated."

In a prepared statement, McMorris said, "It's exciting now to see our work leading to a new family of anti-tumor drug candidates," and Kelner added, "Progress from the Stages I and II of clinical trials by the National Cancer Institute and MGI-Pharma appears excellent, especially relating to cancer of the pancreas, ovaries, and in some cases, the prostate — which are among three of the most difficult cancers to treat."

The results of interim Phase II testing showed that of 36 pancreatic cancer patients, seven achieved a six-month survival benefit, one experienced an 84-percent decrease in tumor mass, and one achieved a complete response to the irofulven treatment.

In the human body, cells shut themselves down or commit "cell suicide" when they sense they are damaged. This applies to both good cells and bad. The reason irofulven has been successful thus far is that it is rapidly absorbed by tumor cells, where it then binds to tumor cell DNA, and won't allow the cell to replicate. This not only stops tumor growth, but tumors actually shrink when the cells figure out that they are damaged and then shut themselves down.

Irofulven side effects are common to other forms of chemotherapy, with the most prevalent being nausea, vomiting, fatigue and bone marrow suppression.