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Silicon medicines may be effective in humans

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As carbon-based life forms, humans and other animals, invariably, are treated for disease with the help of carbon-based medicines. But now, in a promising new study, scientists have shown that silicon — the stuff of computer chips, glass and pottery — may have extraordinary therapeutic value for treating human disease.

"All medicines are carbon-based — like we are," says Robert West, a University of Wisconsin-Madison chemist and one of the world's leading authorities on silicon chemistry. "There are about 50,000 biologically active molecules, and they're all mainly carbon-based."

But now, West and his colleagues report in the January edition of the journal *Silicon Chemistry* that the effectiveness and safety of an important anti-inflammatory and anti-cancer drug were enhanced remarkably by replacing one of the molecule's carbon atoms with a silicon atom.

The drug, indomethacin, is used to treat arthritis and some cancers, but the drug is little used because it is quite toxic.

"Our thought was, maybe we could tame it," says West, a UW-Madison professor of chemistry.

The idea, according to West and colleague Galina Bikzhanova, was to make a simple chemical change to see if the biological properties of the drug could be modified to be safer and more effective. By trading one of the drug's carbon atoms for a silicon atom and exposing the modified

agent to cancer cells in culture, West's group found that the molecule's effectiveness was enhanced and its toxicity greatly reduced.

Indomethacin is an anti-inflammatory drug belonging to a family of compounds known as COX inhibitors. COX inhibitors selectively block an enzyme that causes pain and swelling.

"Our molecule is a COX-2 inhibitor like Tylenol and Vioxx and other such drugs," notes West.

How the drug and other COX inhibitors work against cancer is not well understood, but they clearly demonstrate anti-cancer properties, according to West. The modified molecule with the silicon atom was exposed to several types of cancer cells in culture in the new study. The agent had significant effects on skin and prostate cancer cells, but showed the greatest efficacy against pancreatic cancer cells.

"The results are very promising, especially in using our compound in combination with standard anticancer drugs," says West, who conducted the study in collaboration with Bikzhanova, Irina Toulokhonova of UW-Madison and Stephen Gately of RND Pharmaceuticals in Scottsdale, Ariz.

Tested on cancer cells in cultures, the modified drug both slowed the growth of cancer cells and killed cancer cells directly. The high activity was against pancreatic cancer cells. This is important because pancreatic cancer responds poorly to any therapy and is almost always fatal because it is hard to detect and spreads rapidly.

Perhaps just as important, the silicon-modified molecule exhibited far less toxicity than the all-carbon-based form of the drug.

"We tested for toxicity and it is well tolerated," West explains. "That's

really different than indomethacin and the other indomethacin derivatives that have been made."

West and his colleagues made four variants of the drug, each with a slightly different chemical structure but all containing the silicon atom.

Why does silicon have this effect?

"It changes the property of the molecule, but not drastically," the Wisconsin chemist explains.

"It's fine tuning," says Bikzhanova. "We don't know why, but it led to this unexpectedly strong effect against cancer cells."

Source: University of Wisconsin-Madison