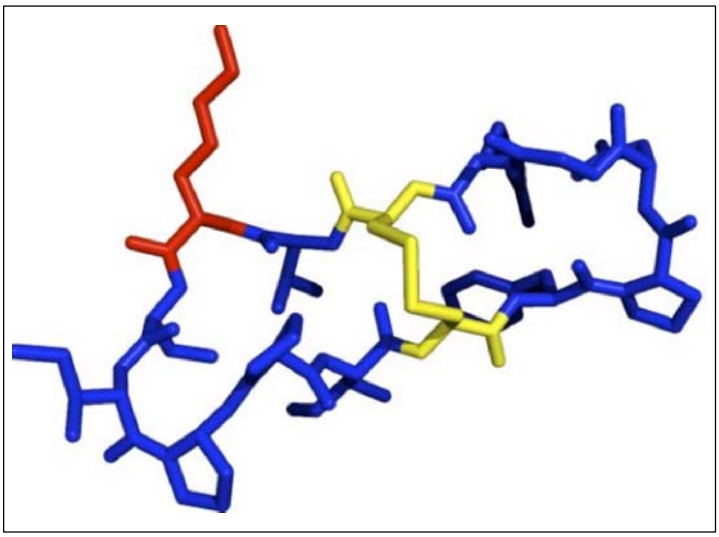
Sunflower's

Hidden Medical Molecule

Cancer Drug Designers Very Interested in Protein Found in Sunflower Plant

By Joshua Mylne



This graphic depicts the circular protein SFTI from sunflower seeds. The protruding arm targeted by the digestive enzyme trypsin is shown in red. SFTI's internal cross-brace is shown in yellow. Thanks to its shape and stability, SFTI blocks trypsin with great potency and is being developed by drug designers to block similar enzymes involved in cancer.

Sunflower seeds are well known for their oil, but very few people know about a tiny and unusual protein in sunflower seeds that's of great interest to chemists and drug designers. The name of this tiny protein is SFTI, for SunFlower Trypsin Inhibitor, and it was discovered in 1999 by a group in Britain.

What's so unusual about SFTI is that it's a circular protein with no beginning and no end. When a protein chain is made, usually each unit is joined head-to-tail, leaving a free head on the first link and a free tail on the last. SFTI not only has no free head or tail; it is also cross-braced by a strong internal bond and is extremely rigid. All these properties make SFTI an extremely stable molecule.

SFTI was discovered because of its ability to block an important digestive enzyme from mammals called trypsin. Trypsin is secreted after food has left the stomach, and its job is to cut up proteins into smaller pieces so they can then be absorbed into the bloodstream. SFTI masquerades as the perfect target for trypsin; but once the enzyme sinks its teeth in, it can't cut SFTI, and so its release is blocked. This ability to block and inhibit trypsin is how SFTI got its name.

The stability of SFTI and its ability to block enzymes like trypsin make it of great interest to cancer drug designers. In cancer, the sufferers' own digestive enzymes are exuded by a tumor to eat into the surrounding flesh and create space for the tumor to grow into. Researchers therefore wish to create drugs that block protein-digesting enzymes such as trypsin in an effort to treat cancer by preventing tumor growth.

In its natural state, SFTI blocks a digestive enzyme involved in breast cancer, and patents have been filed for its use in this way. Drug designers also make slightly different versions of SFTI that target different sites, which allows the new versions to block different enzymes. Recently, three changes to SFTI allowed it to block a digestive enzyme used by prostate cancer.

Drug designers also use SFTI in a completely different way: to protect protein drugs from being broken down. The small protein drug is joined in to the SFTI circular chain, making it hard to be digested. This is a way to overcome the biggest challenge all protein drugs face: being broken down by the patient's own digestive enzymes.

So what's SFTI doing for sunflower seeds? Put simply, it's not entirely clear. Scientists often use trypsin from cattle to help find blockers of digestive enzymes because cattle trypsin is cheap and easy to work with. This means a lot of trypsin inhibitors have been discovered, but none quite so stable and potent as SFTI. It's

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thought these digestive enzyme blockers help protect seeds from being eaten by insects by reducing the nutritional value of any protein the insect gains from eating the seed. But insect digestive enzymes vary greatly and are unlikely to always be blocked as effectively as trypsin.

The original finding of SFTI's ability to block the major digestive enzyme of cattle and its extraordinary stability still stands, and with 350,000 metric tons of crushed sunflower meal heading for livestock feedlots each year in the United States alone, mostly to cattle, it would be interesting to know if it has any effect on them.

Sunflower SFTI is another example of nature making some of the best medicines!

SFTI is water-loving, so it stays in the meal when sunflower is crushed for its oil. Whether SFTI is able to survive being eaten and passed through the digestive system is relevant for its use as a drug, too. The best drugs are ones that can be swallowed; but most proteins don't make it far and are broken down in the stomach. Recently, a protein drug was made circular and shown to exert its pain-killing effect on rats after they ate it in their food, which suggests the circular protein drug passed unharmed through the rat digestive system.

One-third of all current medicines are made either by plants or synthetic molecules that look a lot like plant products. Sunflower SFTI is yet another example of nature making some of the very best medicines! ■

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