# Milk thistle extract stops lung cancer in mice

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Tissue with wound-like conditions allows tumors to grow and spread. In mouse lung cancer cells, treatment with silibinin, a major component of milk thistle, removed the molecular billboards that signal these wound-like conditions and so stopped the spread of these lung cancers, according to a recent study published in the journal Molecular Carcinogenesis.

Though the natural extract has been used for more than 2,000 years, mostly to treat disorders of the liver and gallbladder, this is one of the first carefully controlled and reported studies to find benefit.

Here is how it works:

Basically, in a cell there can be a chain of signals, one leading to the next, to the next, and eventually to an end product. And so if you would like to eliminate an end product, you may look to break a link in the signaling chain that leads to it. The end products COX2 and iNOS are enzymes involved with the inflammatory response to perceived wounds – both can aid tumor growth. Far upstream in the signaling chain that leads to these unwanted enzymes are STAT1 and STAT3. These transcription factors allow the blueprint of DNA to bind with proteins that continue the signal cascade, eventually leading to the production of harmful COX2 and iNOS.

Stop STAT1 and STAT3 and you break the chain that leads to COX2 and iNOS – and the growth of lung tumors along with them.

"This relatively nontoxic substance – a derivative of milk thistle, called silibinin – was able to inhibit the upstream signals that lead to the expression of COX2 and iNOS," says Alpna Tyagi, PhD, investigator at the University of Colorado Cancer Center and member of the Agarwal Lab at the Skaggs School of Pharmacy and Pharmaceutical Sciences.

In addition, Tyagi and collaborators compared the effects of silibinin to drugs currently in clinical trials for lung cancer. Would drugs that target other signaling pathways – other linked chains – similarly cut into the production of COX2 and iNOS?

It turned out that inhibiting the chains of JAK1/2 and MEK in combination and also inhibiting the signaling pathways of EGFR and NF-kB in combination blocked the ability of STAT1 and STAT3 to trap the energy they needed to eventually signal COX2 and iNOS production.

Compared to these multi-million dollar drugs, naturally-occurring silibinin blocked not only the expression of COX2 and iNOS, but also the migration of existing lung cancer cells.

"What we showed is that STAT1 and STAT3 may be promising therapeutic targets in the treatment of lung cancer, no matter how you target them," Tyagi says. "And also that naturally-derived products like silibinin may be as effective as today's best treatments."

Provided by University of Colorado Denver