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## **More fish oil, less vegetable oil, better for your health**

Bethesda, Md. · Scientists have provided new evidence that using more fish oil than vegetable oil in the diet decreases the formation of chemicals called prostanoids, which, when produced in excess, increase inflammation in various tissues and organs. The results, by William L. Smith, Professor and Chair of Biological Chemistry at the University of Michigan, Ann Arbor, and colleagues, may help in designing new anti-inflammatory drugs with fewer side effects than the ones currently available.

Prostanoids help control blood pressure, fight allergies, and modulate inflammation, but too much of them · especially those made from vegetable oils · can also lead to increased pain, swelling, and redness in various tissues, · Smith says. Our study shows that prostanoids made from fish oil are less effective at causing pain and swelling than those made from vegetable oil and that adding fish oil to the diet decreases the amount of prostanoids made from vegetable oil. ·

The new study, to be published in the August 3 issue of the [Journal of Biological Chemistry](#) , was selected as a paper of the Week by the journal's editors, meaning that it belongs to the top one percent of papers reviewed in significance and overall importance.

Smith and colleagues looked at the mutual effects of both oils by changing their respective amounts in cultured cells. As expected, a relative increase in fish oil lowered the amount of prostanoids from vegetable oil, although not always in the expected proportions.

Both fish and vegetable oils are converted into prostanoids through chemical reactions that are aided by enzymes called cyclo-oxygenases (COX), two types of which · COX-1 and COX-2 · are involved in the reactions. The scientists showed that, in reactions involving COX-1, when more fish oil is present, it preferentially binds to COX-1, thus limiting vegetable oil's access to this enzyme. But in reactions involving COX-2, increasing the amount of fish oil did not change the way it binds to COX-2, so a significant portion of vegetable oil was still converted to prostanoids.

This was completely unexpected, Smith says. This new result shows that COX-2 does not prefer fish oil to vegetable oil. Regardless of the amount of extra fish oil that we added, COX-2 still helped convert all the vegetable oil available.

This finding reveals for the first time a limit to how the body naturally regulates levels of prostanoids produced by fish and vegetable oil. If both oil types are present in the body, levels of prostanoids from fish oil will, in general, be higher than those coming from vegetable oil, but mechanisms such as the one involving COX-2 can counter this trend.

The researchers are now investigating why COX-1 and COX-2 act differently. One possibility is that since COX-2 has two binding sites, it can bind to both fish and vegetable oils. When fish oil binds to one of the two sites, it may prepare the other site to bind more easily to vegetable oil, a process called allostery.

Smith and his colleagues hope that by further investigating how prostanoids are regulated in the body, they can design potential drugs that bind to COX-2 and decrease levels of the vegetable oil prostanoids.

The drugs that are currently used to inhibit COX-1 and COX-2 provide relief from the symptoms of inflammation and pain, but they still have many side effects, Smith says. By better understanding how prostanoids work at the cellular level, we hope to find new ways to regulate inflammation and create better anti-inflammatory drugs.

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ARTICLE: Enzymes and Receptors of Prostaglandin Pathways with Arachidonic Acid- vs. Eicosapentaenoic Acid-Derived Substrates and Products, by Masayuki Wada, Cynthia J. DeLong, Yu H. Hong, Caroline J. Rieke, Inseok Song, Ranjinder S. Sidhu, Chong Yuan, Mark Warnock, Alvin H. Schmaier, Chieko Yokoyama, Emer M. Smyth, Stephen J. Wilson, Garret A. FitzGerald, R. Michael Garavito, De Xin Sui, John W. Regan and William L. Smith

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