

Newly discovered anti-inflammatory substances may potentially treat variety of diseases

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Researchers have discovered a new family of substances which has been found to display highly potent activity against the release of proinflammatory cytokines and the toxicity induced by reactive oxygen species (ROS). The novel compounds synthesized and evaluated belong to a family of low molecular weight substances named indolines. In early experiments, these compounds have shown promising activity in the treatment of acute pancreatic inflammation, acute fatty liver damage, and diabetes.

Inflammation, and in particular chronic inflammation, are major contributors to a large number of diseases, such as cancer, acute pancreatic inflammation, fatty liver disease, diabetes, ulcerative colitis, Crohn's disease, rheumatoid arthritis, chronic liver disease, atherosclerosis, multiple sclerosis, and many others. These pathological conditions are associated with the release of substances, known as pro-inflammatory cytokines, by the immune system. These substances participate in the neutralization of invading pathogens, repair injured tissues, and promote wound healing. However, during chronic or excessive activation of the immune system, when these cytokines are released in an uncontrolled manner, they can lead to unnecessary inflammation that frequently causes tissue damage.

In addition, a family of substances, designated as reactive oxygen species (ROS) is also among the major contributors to many chronic diseases. ROS are involved in oxidation processes. Although oxidative reactions catalyzed by ROS are of great importance in metabolic processes and removal of toxic substances from the body, they are also involved in major damage to cells and tissues leading to cell death, possible DNA mutations and aging. Though the presence of oxygen is

necessary for maintaining life, oxygen and its derived products (ROS) are involved in a variety of toxic effects. It has been said that "without oxygen we die but <u>oxygen</u> kills us".

Prof. Abraham Nudelman and his graduate student Shani Zeeli, from the Department of Chemistry at Bar-Ilan University, in collaboration with Prof. Marta Weinstock and her students and assistants from the School of Pharmacy at the Hebrew University, have discovered a new family of substances which has been found to display highly potent activity against the release of pro-inflammatory cytokines and the toxicity induced by ROS. Their findings were recently published in the *Journal of Medicinal Chemistry*, and in other early papers.

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"It is expected that further studies in humans will reveal the potential usefulness of these <u>substances</u> in the treatment of a variety of diseases where inflammation is a major contributor to the disease," says Prof. Nudelman, a lead author of the paper. Further studies on the influence of these compounds on these diseases, and other pathological conditions, are being conducted.

More information: Shani Zeeli et al, Synthesis and Biological Evaluation of Derivatives of Indoline as Highly Potent Antioxidant and Anti-inflammatory Agents, *Journal of Medicinal Chemistry* (2018). DOI: 10.1021/acs.jmedchem.8b00001



Provided by Bar-Ilan University

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