**NIH-AARP NSAIDS and Melanoma Risk**

Contents

[Elkeeb D. 2012, Photosensitivity: a current biological overview 2](#_Toc452465297)

[The mechanism of action of aspirin 3](#_Toc452465298)

## Elkeeb D., 2012: Photosensitivity: a current biological overview

[link](http://www.tandfonline.com/doi/full/10.3109/15569527.2012.656293)

Exogenous photosensitivity

* 1. Phototoxicity
  2. Phototoxicity is acute toxic response from light that is non-immunologic, either directly or systemically from photosensitizers
  3. Adequate doses of the agent (photosensitizer) and radiation (sunlight, UV lamp) are required for the reaction
  4. Photoirritation is a phototoxic reaction from topical application of photosensitizers 0-72 hours after exposure to light/UV
  5. Photosensitizers include: NSAIDS, antimicrobials, antihypertensive, diuretics, and anticonvulsants

1. Mechanism of phototoxicity
   1. Photodynamic reactions
      1. Light excites electrons in the photosensitizer and creates unstable energy states, and releases energy to surrounding cells when the electrons fall back to their ground state
      2. Type I reactions damage cell components (nucleic acids, lipids, and protein) by reacting with oxygen to form free radicals
      3. Type II reactions produce singlet oxygen which then oxidizes cell components
   2. Non-photodynamic reactions
      1. Non-photodynamic chemicals/drugs can cause damage without using oxygen
      2. Example is psoralens such as 8-methoxypsoralen
      3. The molecules interculate with DNA, and with photoactivation, those molecules result in mono- or bifunctional adducts with DNA, depending on structure of the molecule
2. Photoallergy
   1. Unlike phototoxicity, photoallergy has an immunologically mediated component to the reaction through the formation of a photosensitizer-protein conjugate
   2. Examples include: promethazine, benzocaine, p-aminobenzoic acid
   3. Can result from topical or systemic photosensitizer with onset usually delayed 24 hours to several days

## Vane J.R., 2003: The mechanism of action of aspirin

[link](http://www.sciencedirect.com/science/article/pii/S0049384803003797)

1. Brief History
   1. In 1874, Kolbe and colleagues formulated salicylic acid to form Heyden Chemical Company
   2. 1895, Felix Hoffman, working for Frederick Bayer, searched for a derivative of salicylic acid
      1. Hoffman discovered acetylating the hydroxyl group on the benzene ring of salicylic acid
      2. The process produced acetylsalicylic acid, named “aspirin” by Bayer’s chief pharmacologist, Heinrich Dreser
   3. Aspirin’s mechanisms anti-inflammatory and analgesic mechanisms unknown until 1971
      1. Vane and colleagues investigated prostaglandin after examining RCS (thromboxane)
      2. Vane published [results](http://www.nature.com/nature-newbio/journal/v231/n25/pdf/newbio231232a0.pdf) in Nature in 1971, showing dose-dependent inhibition of prostaglandin
   4. Aspirin acetylates hydroxyl group of one serine residue (Ser 530) located 70 amino acids from the C terminus of the cyclooxygenase enzyme
      1. Acetylation of the cyclooxygenase enzyme is irreversible