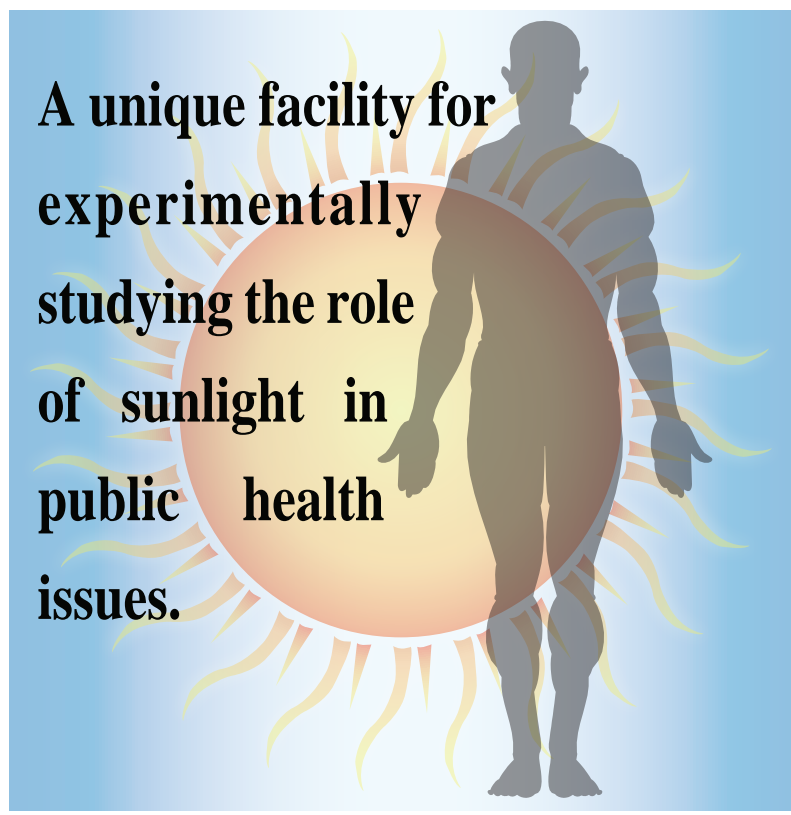




PHOTOTOXICOLOGY



A unique facility for experimentally studying the role of sunlight in public health issues.

Jointly sponsored by the National Toxicology Program and the U.S. Food and Drug Administration



Providing:

- *In vivo* exposure of animals to simulated solar light
- *In vivo* exposure of animals to ultraviolet (UVA or UVB) light
- *In vitro* studies using defined light sources

Why the concern regarding light?

Humans are exposed to sunlight every day. The dose of sunlight received depends on many self-determined factors, such as the amount of time spent outdoors, the type of clothing worn, and the use of sun-protection (hats or sunscreens). Exposure to the ultraviolet radiation (UVR) component of sunlight is known to cause adverse effects in humans ranging from sunburn (acute effects) to skin cancer and cataracts (long-term effects). The dose of UVR received from sunlight varies depending on the time of day and the solar zenith angle (the latitude and time of year). Therefore, understanding the toxicological risk and interaction of UVR with plant toxins and drugs or pollutants should increase our ability to control or reduce public health risk to the combination of UVR with these substances.



Center for Phototoxicology History

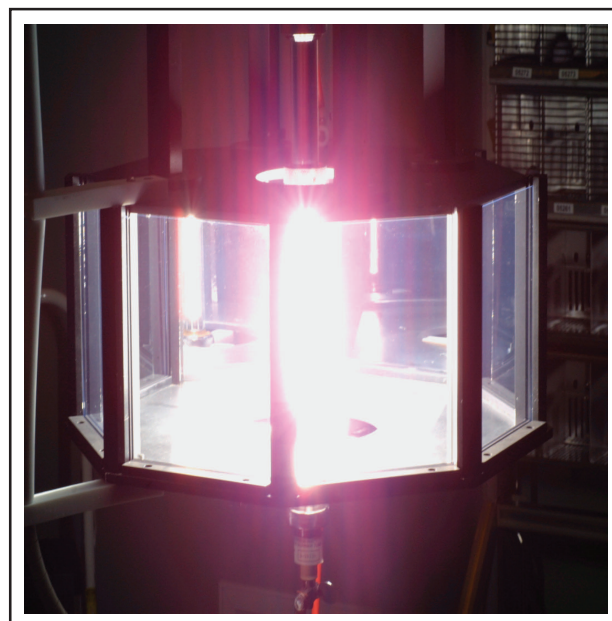
The National Center for Toxicological Research (NCTR) was established in 1971 in Jefferson, Ark. NCTR is one of the six Centers of the U.S. Food and Drug Administration (FDA) with a mission to “... *conduct peer-reviewed scientific research that supports the FDA’s current regulatory mission, and anticipates future regulatory needs.*” The National Toxicology Program (NTP), located at the National Institute for Environmental Health Sciences in Research Triangle Park, N.C., was established in 1978 with a mission “... *to coordinate government toxicology testing programs, strengthen the science base in toxicology, develop testing methods, and quantify the health risk of potentially toxic chemicals and materials to which the U.S. public is exposed.*” The NTP Center for Phototoxicology was created at the NCTR in 2000 to enhance the capabilities of NCTR and NTP to address the role of terrestrial sunlight on the toxicity and carcinogenicity of chemicals. This facility was additionally envisioned as a resource for government agencies and academic institutions for examining the role of sunlight in biological processes, toxicity, or carcinogenicity.



Simulated Solar Light Generation

The core feature of the Center for Phototoxicology is two 6,500 watt xenon arc simulated solar lights with spectral emissions similar to extraterrestrial sunlight. Quartz glass filters are used to remove unwanted light below 295 nm, resulting in a spectrum that is representative of terrestrial sunlight. By modifying the filters, the transmitted light can be selected that matches a desired spectrum, such as a specific latitude, season, or ozone concentration.

In addition to xenon arc solar simulated light, the Center for Phototoxicology uses fluorescent lamps to generate light that is either predominantly UVB or UVA. The choice of light sources depends on the experimental design.



Experimental Designs

The types of acute and chronic (up to one year) studies that are conducted in the facility include:

- Phototoxicity**—quantifying the toxicity of a chemical following irradiation with light source;
- Photocarcinogenicity**—quantifying the carcinogenicity of a chemical following exposure to a light source;
- Photocarcinogenicity**—quantifying the effect of a chemical on the carcinogenicity of UVB-containing light source.

In a photocarcinogenicity study, the mice are treated 40 weeks with doses of UVR that induce skin tumors, and the effects of prior, post, or coincident exposure to a chemical on tumor formation are quantified. In addition, some studies are supported by **mechanistic studies**, such as chemical or photoproduct quantification, biomarker quantification (DNA adducts or mutations), RNA expression (genomics), and protein expression (proteomics). Studies are typically conducted under Good Laboratory Practices (**GLP**).

Test Animals

The facility is equipped primarily for mice, although other species could be accommodated. Typically, hairless mice, especially the SKH-1 (hr⁻/hr⁻), have been used in photocarcinogenicity and photocarcinogenicity studies. Any animal model (such as the transgenic Tyr-H-*ras* (+), Ink4a/Arf (-/-) mouse) can be used to study the role of UV in melanoma induction.

Test Facilities

The Center for Photoxicology contains:

Light Sources:

- 2 independent 6.5 kW solar light simulators (fixed, horizontal exposure)
- 6.5 kW solar simulator (portable, vertical exposure)
- 2,500 UVB-fluorescent lamp source (portable, horizontal exposure)
- 800 watt UVB-fluorescent lamp source (portable, vertical exposure)
- 2,500 watt UVA-fluorescent lamp source (portable, horizontal exposure)
- 800 watt UVA-fluorescent lamp source (portable, vertical exposure)
- Class IV Nd:YAG laser (mechanistic studies only)

Animal Husbandry:

- 6 animal housing rooms with automated water system (maximum of 14 racks)
- 6 additional rooms available with no automated water
- 92 custom animal housing/exposure racks with automatic water system (72 mice/rack)
- Edstrom Industries automatic water system for animal racks

Light Dosimetry:

- Optronics OL-754 Spectroradiometer
- Custom individual animal rack dosimetry system (broadband dosimeters)

Clinical Metrics During Study:

- Animal weight (weekly)
- Digital image of dosed skin for tumor location, multiplicity, and size (weekly)

NCTR Study Support:

- Animal breeding facility
- Animal quarantine facility
- Diet preparation facility (dosed feed and water)
- Chemistry support for dose certification
- Animal database tracking system (NCTR developed MultiGen)
- Microbiology support for hygiene
- Pathology facilities (necropsy, frozen sections, histochemistry, immunohistochemistry, and Aperio Scan Scope for digital images of all slides)
- Statistical support
- NCTR Quality Assurance Unit (for GLP studies)
- NCTR genomics, proteomics, metabolomics support

The Center for Phototoxicology is a national resource where research partnerships can be established. Mechanisms used to support studies in The Center for Phototoxicology have included **Interagency Agreements (IAGs)** between U.S. government agencies and **Cooperative Research and Development Agreements (CRADAs)** between FDA and nongovernment entities.

Recently Completed Project

Alpha and Beta Hydroxy Acids

Photocarcinogenicity study of topically applied glycolic acid (alpha hydroxy acid) and salicylic acid (beta hydroxy acid) using simulated solar light on SKH-1 mice. Reported in NTP Technical Report 524.

Current Projects

Aloe Vera

Photocarcinogenicity study of various topically applied *Aloe vera* plant components using simulated solar light on SKH-1 mice. NTP Technical Report expected in late 2006.

Retinyl Palmitate

Mechanistic and photocarcinogenicity study of topically applied retinyl palmitate using simulated solar light, UVB, and UVA light on SKH-1 mice. NTP Technical Report expected in late 2007.

Tattoo Inks

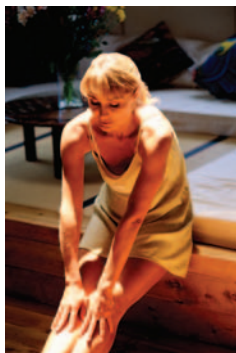
Mechanistic and photocarcinogenicity studies of several tattoo ink pigments using simulated solar light on SKH-1 mice.

Melanoma Animal Model

Photocarcinogenesis study using Tyr-H-ras (+), Ink4a/Arf (-/-) transgenic mouse, and UVB light.

Dermal Penetration of Nanoscale Materials

The dermal penetration of nanoscale quantum dots and titanium dioxide, a component of certain sunscreens and other cosmetic products, using SKH-1 mice and Tg.AC transgenic mice.



April 5, 2006



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