



Photosensitizers

By Carolina Soehnchen and Anna Richter

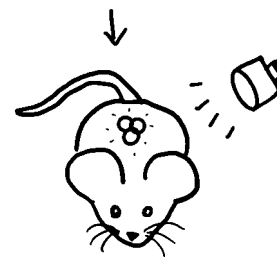
Introduction to “Photosensitizer”

- Photosensitizer initiate chemical change in another molecule in a photochemical process
- Works through **absorption** of electromagnetic radiation to transfer it to adjacent molecules
- Common example is **chlorophyll** acting in plants during photosynthesis
- Division: porphyrins, chlorophylls and dyes
- Medical use in **photodynamic therapy** for treatment of cancer:
 - production of singlet oxygen which act cytotoxic on cancer cells
 - Often combined with chemotherapy, radiotherapy, immunotherapy, or even herbal medicine therapy



Inactive photosensitizer

|
administration



Activated photosensitizer

|
O₂ from tissue



Cytotoxic effect

Characteristics of ideal photosensitizer

1. Relatively **easy attainment**
2. Lack of toxicity in dark conditions
3. **Solubility** and stability in aqueous solutions
4. High absorption coefficient within the range of 600-800 nm where light penetration of tissue is maximal
5. Existence of high quantum yields for triplet state formation and production of reactive oxygen species
6. Binding to intracellular locationions that are highly sensitive to oxidative damage
7. Selective **absorption** into target tissue
8. Ability to be excreted from the body, in order to avoid posttreatment phototoxicity
9. **Optimum pharmacokinetic properties**
10. Short drug light interval to facilitate outpatient treatment
11. No toxic effect on healthy tissues and organs

Pheophorbide A

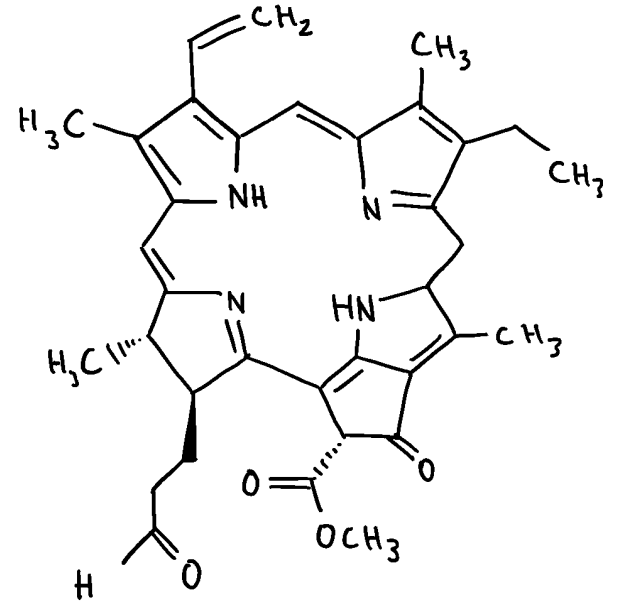
Product of: chlorophyll of green plants

Absorption wavelength: 410-668 nm

Cellular target: mitochondria

Indications:

- Production of high levels of reactive oxygen species
- Phototoxic effects: human colorectal adenocarcinoma, human hepatocellular carcinoma, human uterine sarcoma cell lines



Curcumin

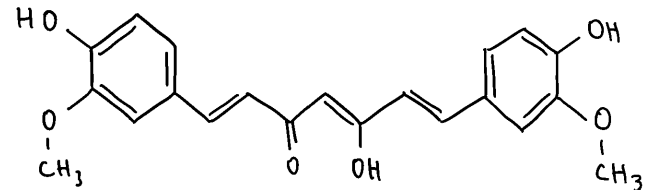
Product of: rhizome of *curcuma longa*

Absorption wavelength: 350 to 450 nm

Cellular target: lysosomal membrane

Indications:

- Shows antioxidant, anti-inflammatory and anticancer effects
- Acts cytotoxic against neural progenitor cells



Anthraquinones

Product of: rubiaceae (family of flowering plants)

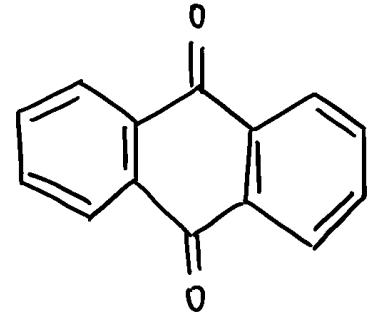
Isolation of: rubiadin 1-methyl ether, damnacanthal, soranjidiol, postuline, damnacanthol, and heterophylline

Absorption wavelength: 220- 440 nm

Cellular target: mitochondria

Indications:

- Used against caspase-3-transfected human breast carcinoma cells (MCF-7)



Thiophenes

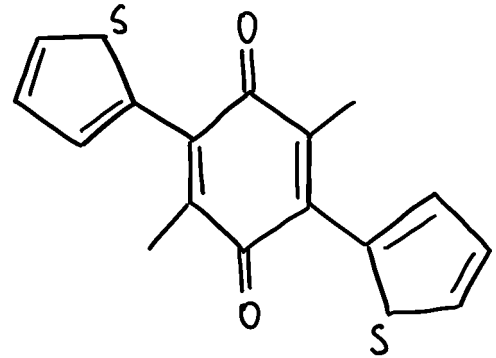
Product of: Echinops latifolius Tausch (flower)

Absorption wavelength: 225 and 400 nm

Cellular target: lysosome

Indications:

- Cytotoxic effect on human cancer such as skin (A375-S2) and cervix cancer (HeLa)



15(1)-Hydroxypurpurin-7-lactone ethyl methyl diester

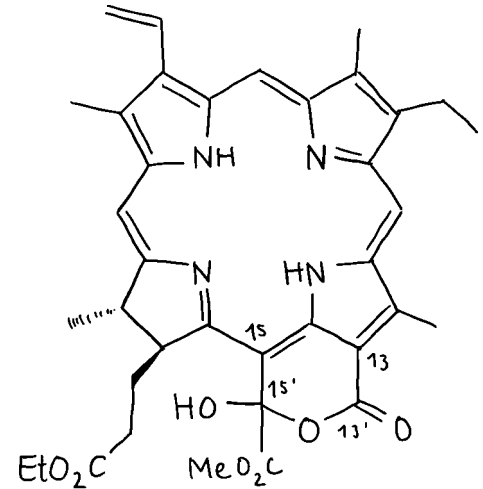
Product of: Araceae or leaves of bamboo plants

Absorption wavelength: ~700 nm

Cellular target: not identified

Indications:

- Induces apoptosis in human leukemic cells (CMK-7)
- Shows phototoxic effect in oral (HSC2) and nasopharyngeal (HK1) cancer



Aloe-emodin

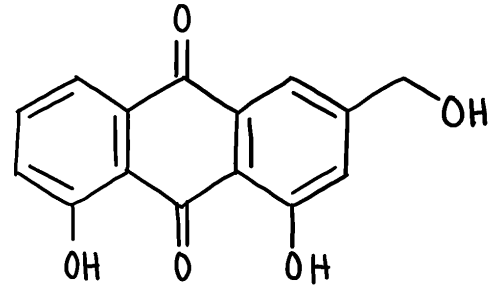
Product of: Aloe vera roots

Absorption wavelength: 370-500 nm

Cellular target: lysosome

Indications:

- Acts anti-angiogenic
- Used in treatment against osteosarcoma (U2OS) and fibrosarcoma (HT-1080) cells



To1yporphin

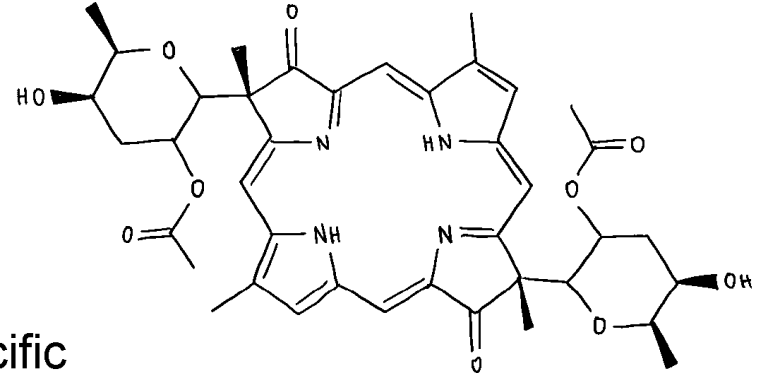
Product of: cyanobacteria

Absorption wavelength: 676 nm

Cellular target: perinuclear region and specific vesicles

Indications:

- Used in treatment of metastasis



Chlorophyllin

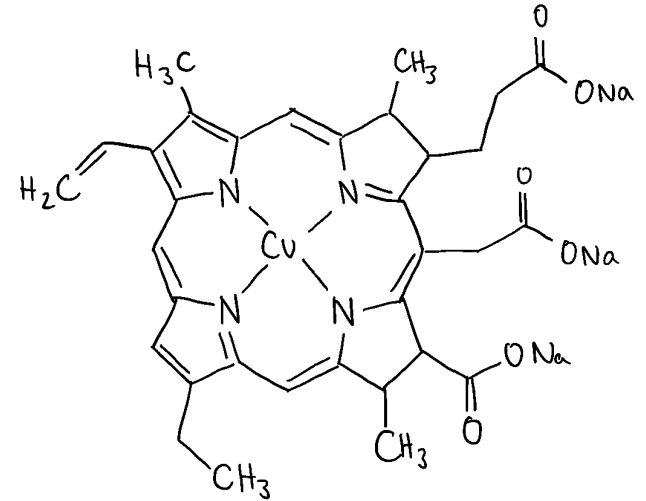
Product of: cyanobacteria and chloroplasts of algae and plants

Absorption wavelength: 600-670 nm

Cellular target: lysosomes and mitochondria

Indications:

- Used in treatment of bladder cancer, breast cancer, melanoma



Hypericin

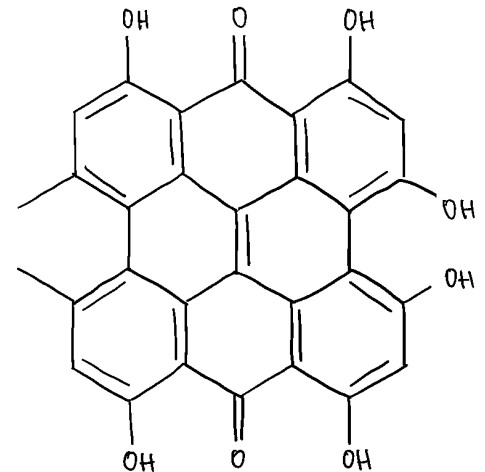
Product of: Hypericum perforatum (yellow flowering herb)

Absorption wavelength: 524- 593 nm

Cellular target: membranes of nuclear, endoplasmic reticulum (ER), Golgi complex and mitochondria

Indications:

- Has excellent clinical photodynamic properties
- Used in treatment of bladder cancer, nasopharyngeal carcinoma cells



Hypocrellin A/B

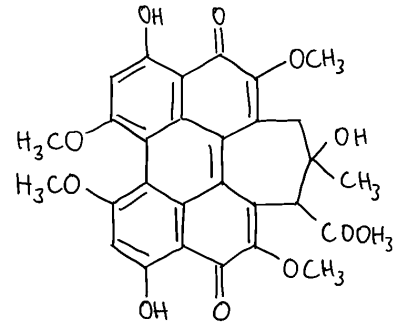
Product of: Hypocrella bambusae (parasitic fungus)

Absorption wavelength: < 600 nm and ~ 470 nm

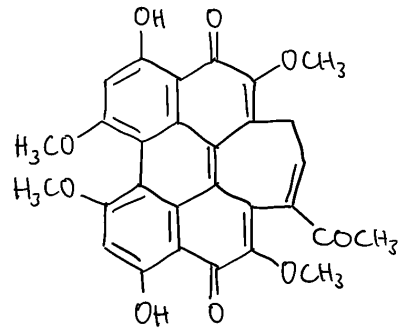
Cellular target: Lysosomal compartment, mitochondria and cell membranes

Indications:

- Is lipophilic causing aggregation in blood plasma
- Used in treatment of skin diseases and cervical cancer



A



B

Cercosporin

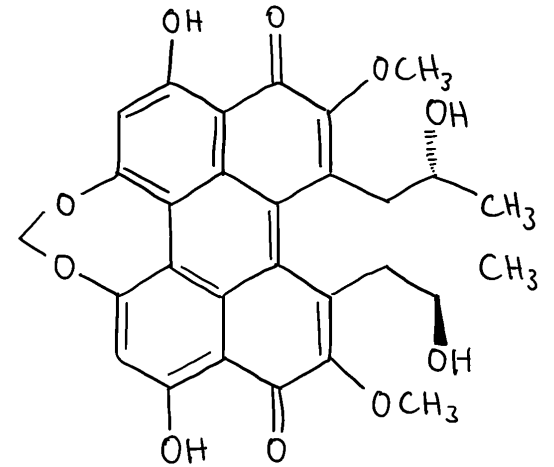
Product of: *Cercospora kikuchii* (fungi)

Absorption wavelength: < 532 nm

Cellular target: mitochondria and endoplasmic reticulum

Indications:

- Used in the treatment of glioblastoma multiforme, breast adenocarcinoma
- Has poor water solubility properties



Hypericum perforatum (HP)

Hypericin a compound isolated from *Hypericum perforatum* (HP), the potential to be utilized as first choice for PS.

→ Studies: phototoxic effect of hypericin can be multiplied by combination with other PS's such as chlorine (e6) excited by white light, and hyperthermia can be used.

◆ Apoptosis is induced by mitochondrial pathway

Include: caspase-3, caspase-9, and cell growth is inhibited by suppression of activation of vascular endothelial growth factor-A (VEGF-A)-mediated PI3K/Akt pathway

Traditional Chinese Herbs

- A study by Liao Jing et al.: PS compounds extracted were introduced with fluorescence properties.
 - ◆ reduce the metabolic cell viability, proliferative ability, and increase cell death
- Herbs: Radix bupleuri, Rhizoma polygoni cuspidati, Rabdosia rubescens, Cortex magnoliae officinalis, and Rhizoma chuanxiong,
 - ◆ light activation exert an anti-cancer effect via initiation of autophagy
- Compounds: pheophorbide A, tolyporphin, chlorophyllin, curcumin, anthraquinones, hypericin, hypocrellin, cercosporin, thiophenes, 15(1)-hydroxypurpurin-7-lactone ethyl methyl diester, aloe-emodin

Sources

*Presentation made by Carolina Soehnchen and Anna Richter in cooperation with Prof. Dr. Aebisher
University of Rzeszów, Poland*



- Photodynamic therapy for cancer: Role for natural products, *article link:*
<https://pubmed.ncbi.nlm.nih.gov/31063860/>
- Plant extracts as natural photosensitizers in photodynamic therapy: in vitro activity against human mammary adenocarcinoma MCF-7 cells, *article link:*
<https://www.sciencedirect.com/science/article/pii/S2221169116307626>
- St John's Wort (*Hypericum perforatum* L.) photomedicine: hypericin-photodynamic therapy induces metastatic melanoma cell death, *article link:*
<https://pubmed.ncbi.nlm.nih.gov/25076130/>