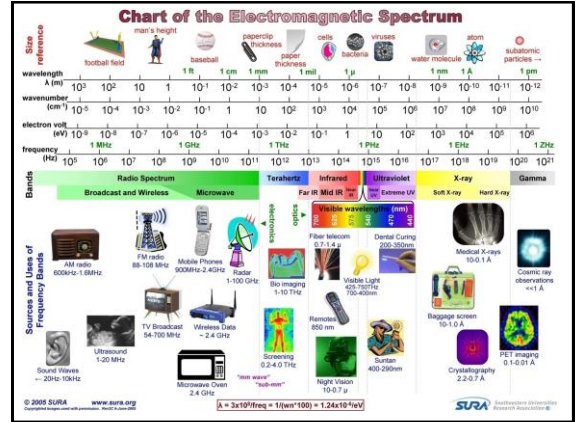


MUNI PHARM

Non-ionizing electromagnetic radiation: The influence of visible light, UV and IR radiation on living organism

Biophysics

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Sources of radiation

- Natural** (stars, atmospheric discharges, luminescence)
- Sun** – ca 30-60% of the radiation is scattered back to the space
 - ca 5-20% of the radiation is absorbed by the atmosphere
- Manifestations of solar energy on Earth-> energy conservation law: Biomass (wood, coal, oil), wind, water cycle, heat
- Artificial**

Incoherent – multiple wavelengths

a) Incandescence – continuous spectrum (eg. bulb, flame)

b) Luminescent – line spectrum (eg. fluorescent tube, LEDs)

Coherent
– one wavelength, the same phase and the same amplitude (**laser**)

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Physical characteristics of visible radiation

- Luminous efficacy K [lm/W]** is a measure how well a light source produces visible light.

Light Source	Luminous Efficacy K [lm/W]
Candle	~0
Bulb	~10
Economy bulb	~50
Fluorescent lamp	~70
High pressure fluorescent lamp	~150

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Physical characteristics of visible radiation

- Luminous flux** $\phi = \frac{\Delta E_s}{\Delta t}$ (lm)
 - It is the light energy that is radiated at time t
- Luminous intensity** $I = \frac{\Delta \phi}{\Delta \Omega}$ (cd)
 - This is the ratio of luminous flux emitted in angle $\Delta \Omega$
- Illuminance** $E = \frac{\Delta \phi}{\Delta S}$ (lx)
 - Is the luminous flux per unit area S
 - Depends on the distance from the source
 - The human eye can register lighting 2 nlx (100 lx is optimal for reading)

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Optical methods

- Optical microscopy** (VIS, UV, IR, polarization, luminescence)
- Absorption spectrometry:**
 - Spectrophotometry (UV/VIS),
 - Fluorescence spectroscopy (aromatic amino acids, porphyrins),
 - Infrared spectroscopy (structure analysis, quality control)
- Polarimetry** (optical active compound)

Optically active samples causes rotation of the plane of polarized light as it passes through the sample.
Optical isomers (e.g. drugs) can have different effects on the body.

Optical active compound are mirror image to each other (enantiomers R and S)

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Optical methods

- Laser diffraction** (particle size determination)
- Nephelometry and turbidimetry** (colloid samples analysis, e.g. determination of albumin and immunoglobulins)

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Optical methods

- Refractometry** (refractive index measuring; e.g. raw materials identification or determination of sample concentration)
- Endoscopy** (optical fibers; looking inside the body for medical)

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LASERS

Light Amplification by Stimulated Emission of Radiation.

- The light is radiated from the laser in the form of a narrow beam; is coherent and monochromatic (usually UV, VIS, IR).
- The principle is the emission of radiation by active particles (atoms, molecules, ions) which are excited by an external energy source. Emitted photons then interact with other electrons of active particles, thereby initiate the stimulated emission of photons.

$$E_2 - E_1 = \Delta E = h\nu$$

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LASERS

According to the **active medium** lasers are divided into:

- Solid state Neodymium etc. (IR – dermatology, eye surgery, stomatology)
- Semiconductor laser diode (surgery, photodynamic therapy)
- Gas CO₂ (IR), He-Ne or Ar (VIS).
- Liquid solutions of organic pigments (coumarin 400-500 nm, xanthene 700-1500 nm)
- and other (e.g. X ray region, microwave region)

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Biological effects of LASERS:

Therapeutic applications

- Invasive therapy** - LASERS energy is over 1 W
 - Surgery** - CO₂ and Nd lasers (IR); tissue is affected only to a depth of 0.1 mm; leads to coagulation of small vessels – the cut does not bleed and is sterile
 - Ophthalmology** - Ar lasers (VIS)
 - photoablation – clean cut, short-wave laser
 - photocoagulation of vascularized tissue (retinopathy treatment)
 - Dermatology** – Ar lasers
 - photocoagulation of vascular lesions, removal of skin pigmentation and warts, depilation, removal of tattoos
 - Stomatology** – Er lasers (IR)
 - treatment of dental caries
 - periodontics (tartar removal, sterilization during inflammatory processes)
 - surgery

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Biological effects of non-ionizing radiation

Sun light:
5% of the ultraviolet, 45 of the infrared and 50 % of the visible variation

- Photosynthesis
- Psychological effects
- Synthesis of vitamin D
- Phototoxic reaction
- Phototherapy

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Biological effects of VIS radiation

Photosynthesis

$$6\text{CO}_2 + 6\text{H}_2\text{O} \xrightarrow{\text{light energy}} \text{C}_6\text{H}_{12}\text{O}_6 + 6\text{O}_2$$

carbon dioxide water glucose oxygen

Granum - a column of thylakoids that have a dye (chlorophyll) embedded in their membrane

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Biological effects of VIS radiation

Photosynthesis

The energy of VIS light causes **excitation of the chlorophyll** molecules. When they are returning to the basic energy levels the **electron is released = photooxidation**.

Secondary phase:
The conversion of **CO₂** into **glucose** using ATP and NADPH from the primary (light) phase - Calvin cycle.

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Biological effects of VIS radiation

- Effect on periodicity of vital functions - **circadian rhythms** (body temperature, blood pressure, hormonal and metabolic processes).
- Effect of color on the **psyche** and perception of the environment (eg. red – excitatory effect, green – calming effect).

Color vision: When white light passes through the transparent material or is reflected by the surface of a solid, a portion of radiation is absorbed. The remaining radiation (appears to us as the color of the object) will have a **color complementary** to the absorbed wavelengths.

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Biological effects of VIS radiation

„Blue light“

The most important part is the blue region of the spectrum - where the body is most sensitive.

- Can lead to disruption of melatonin ("sleep" hormone) biochemistry and it can lead to disruption of circadian biorhythms.

Colour tint of white light:

- warm white (3000 K)
- neutral white (5000 K)
- cool white (7000 K)

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Biological effects of VIS radiation

PHOTOTHERAPY

Use of different wavelengths (including **UV** and **infrared**), **polarized light** and **lasers**. Treatment of skin diseases - inflammations, eczema, bedsores, and others.

- **Acne treatment** (*Propionibacterium acnes* produce porphyrins – photosensitizers)

Photons + Porphyrins

↓

Excited porphyrins molecules and subsequent reaction with O₂

↓

ROS production (superoxide, hydroxyl radical) and *P. acnes* photoinactivation

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Biological effects of VIS radiation

- **Newborn jaundice**
- yellowish discoloration of the skin in a newborn baby.

Causes: the breakdown of fetal hemoglobin (is replaced with adult hemoglobin) and decreased elimination of bilirubin in the liver in newborns.

Treatment: Phototherapy (absorption maximum of bilirubin is 460 nm)
Bilirubin is insoluble and therefore must be converted in the liver to soluble metabolite. Photoisomer (cis-isomer) is soluble and can be eliminated from the body.

Bilirubin Internally H-bonded Water-insoluble

Photoisomers H-bonds to water Increased solubility


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Biological effects of VIS radiation

PHOTODYNAMIC THERAPY

Using of photosensitive substances (photosensitizer). Upon irradiation and excitation, the photosensitizer begins to form reactive oxygen forms (ROS).

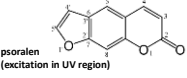
- **Treatment of chronic inflammatory dermatoses**
- Acne treatment
- Psoriasis



5-aminolevulinic acid

NC(=O)CC(O)CC(O)C(=O)O

psoralen
(excitation in UV region)

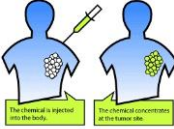


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Biological effects of VIS radiation

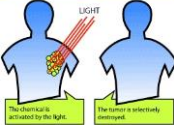
PHOTODYNAMIC THERAPY

- **Treatment of cancer** (porphyrins and their conjugates, treatment of the surface tissues or endoscopic use of laser technology).
- The biggest limitation of photodynamic therapy is the passage of radiation not exceeding 1 cm deep tissue.
- Most commonly used for adjunctive treatment of non-metastatic skin tumors.



The chemical is injected into the body.

The chemical concentrates at the tumor site.



LIGHT

The chemical is activated by the light.

The tumor is effectively destroyed.

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Biological effects of VIS radiation: LASERS

PHOTODYNAMIC THERAPY

- **Therapy of wet macular degeneration**


The drug (porphyrins) intravenous injection. Photoactivation of the drug by laser (689 nm, 80 s) leads to reaction with oxygen and ROS formation and thus damage of irradiated structures (blood vessels).

The cause is the proliferation of newly formed vessels under the retina, these vessels subsequently cause the leakage of blood into the retina and the subsequent edema of the retina.




THE RETINA

ROVILLA, MACULA, OPTIC DISC, CENTRAL RETINAL VEIN, PERIPHERAL RETINAL VEIN, OPTIC NERVE, OPTIC ATTACHMENT



View by healthy eye

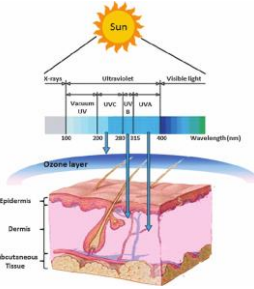


View by eye with the wet macular degeneration

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Ultra-Violet (UV) radiation

- **UV-A (400-315 nm)**: natural tan; mainly responsible for **indirect DNA damage** by the generation of ROS - skin aging
- **UV-B (315-280 nm)**: the so-called middle or erythral; responsible for **direct and indirect DNA damage** – mutagenic; only 1-10 % passes to the earth (ozone, smog, clouds); is filtered by window glass (in contrast to UV-A)
- **UV-C (100-200 nm)**: not passing through the ozone layer



Sun

X-rays, Ultraviolet, Visible light

UVA, UVB, UVC

300 200 100 0 0 100 200 wavelength (nm)

Ozone layer

Epidermis, Dermis, Subcutaneous Tissue

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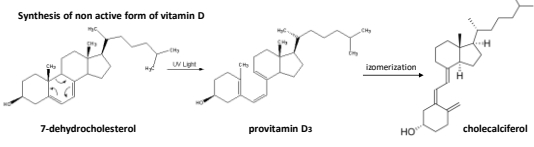
Biological effects of UV radiation

- **Synthesis of vitamin D₃**

Deficiency => defective mineralization of bones (rickets), osteoporosis (decreased bone strength), tooth decay.

Treatment: cholecalciferol + **phototherapy** (UV-B).


Synthesis of non active form of vitamin D



7-dehydrocholesterol

provitamin D₃

cholecalciferol

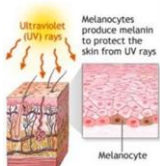


Calcitriol: active form of vitamin D. Is formed from cholecalciferol in liver and kidney (hydroxylation of cholecalciferol molecule). Vitamin D has many physiological functions, such as affecting immunity.

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Biological effects of UV radiation

- **Erythema** – skin redness (mainly due to UV-B); appears about 4 hrs. after exposition, maximum 8-24 hrs. after exposition. Photoprotective function of **melanin** (different types: eumelanin, pheomelanin).




Ultraviolet (UV) rays

Melanocytes produce melanin to protect the skin from UV rays

Melanocyte

If UV rays exceed what can be blocked by your level of melanin, sunburn results



Part of the structure of eumelanin; 2 types: brown and black

O=C1C(=O)N2C(=O)C(=O)N(C2)C(=O)N1C(=O)O


In human skin, melanin production is stimulated mainly at the time DNA damage occurs.

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Biological effects of UV radiation


Skin aging

- Repeated, prolonged exposure of UV radiation
- Loss of elasticity, wrinkles, increased pigmentation.



Solariums and UV radiation

- Mainly UV-A (unlike UV-B does not cause skin redness but penetrates deeper into the skin - skin aging)
- Increased risk of skin melanoma



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Biological effects of UV radiation

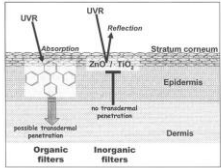
- UV protection: Sunscreens**

Organic compounds – contain chromophores, which absorb UV radiation

- (-) can be a source of ROS
- (-) do not cover the full spectrum of UV-A and UV-B
- (+) colorless, odorless, easy to apply

Anorganic compounds – reflect and scatter UV radiation (ZnO, TiO₂)

- (+) do not form ROS
- (+) protection against UV-A and UV-B
- (-) opaque, worse application



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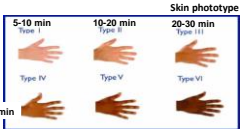
Biological effects of UV radiation

SUN PROTECTION FACTOR (SPF)

- Simply expresses multiple of **time for a relative staying on the sun** without causing solar inflammation with solar skin reddening.
- SPF numbers on a package can range from as low as 2 to as high as 100.

FILTER OF UV RAYS	
SPF 10	90%
SPF 25	95%
SPF 30	96.7%
SPF 60	98.3%

How long can I stay in the sun?
 Example: SPF 15
 Type III (20 min without sunscreen)
 $15 \times 20 = 300 \times 1/2 = 150 \text{ min}$

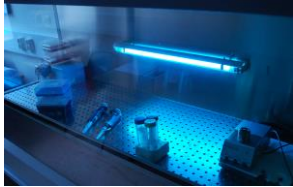


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Biological effects of UV radiation

- UV-C**

-> **germicidal lamps** produce short-wave ultraviolet radiation (below 280 nm), which is bactericidal and virucidal and is used for disinfecting air and surfaces.




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Biological effects of UV radiation on the skin:


Phototoxic reaction

- Phototoxicity is a skin reaction after **local or system application** (oral, parenteral, intravenous, intramuscular, subcutaneous) of the **photoactive drug and subsequent sun exposure**.
- Primarily UV-A** (400-315 nm) - can pass through the glass window.

A) phototoxic reactions



B) photoallergic reactions




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Biological effects of UV radiation on the skin:

Phototoxic reaction

- Non-immunological reaction**
- Does not require previous exposure**
- Dose-dependent**
- Abnormal response to increased sun exposure
- Within several min or hrs after exposure - appears as exaggerated sunburn - erythema, blisters, swelling
- Photodermatitis** - damage to the skin resulting from contact with plants, eg. plant families: Umbelliferaceae, Rutaceae, Compositae



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Biological effects of UV radiation on the skin:

Phototoxic reaction

- The first symptoms often occur already within minutes to hours after irradiation, followed by peeling of the skin and **tendency to permanent hyperpigmentation**.



Phototoxic reaction after contact with perfumed cosmetic product



Movements of pigment; state 6 weeks after treatment

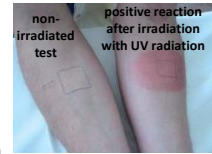
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Biological effects of UV radiation on the skin:

Phototoxic reaction

Some photoactive drug (may induced phototoxic reaction after exposure to sunlight):

- Antibiotics and chemotherapeutics – **tetracyclines, sulfonamides**
- NSAIDs – eg. ketoprofen, diclofenac
 - **Analgesic ointments eg. Fastum Gel, Voltaren**
- Antipsychotic – tricyclic antidepressants
- Heart drugs, drugs affecting the blood vessels
- Diuretics
- Hormonal preparations
- Artificial sweeteners – saccharin
- Antiseptics – chlorhexidine
- Perfumes – Essential oils
- Disinfectants
- Substances of plant origin (herbal medicine)



Epikupal test with ketoprofen

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Biological effects of UV radiation on the skin:

Photoallergic reactions

- Acute or chronic immunological reactions** → UV radiation cause the transformation of a drug to a new substance, eliciting a response of the immune system
- Occurs less commonly than phototoxic reaction (may present as eczematous or sunburn-like reactions)
- Requires previous exposure**
- Independent on the dose**
- Usually induced by topical agents:
 - antibacterial substances
 - topical anti-inflammatory drugs
 - aromatic substances (perfumes)
 - sunscreens



Photoallergic reaction after contact with ketoprofen

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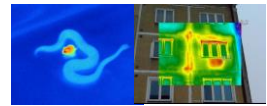
Biological effects of IR radiation

Infrared radiation λ :

near 800-2500 nm, middle 2500 nm-25 μ m, far 25-1000 μ m

Sources:

- natural source Sun, heaters, chem. reaction, geothermal energy

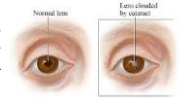


Thermal effects on the skin:

- after absorption of large intensities of IR are irritated heat receptors and later pain receptors (pain threshold ca 45 °C)
- with increasing temperature occurs erythema and later burns

Other effects:

- near IR radiation penetrates the eye and is absorbed by the iris, lens and retina. Can cause **cloudy lens or cataract** (occupational disease – melters, metal workers, glass blowers).



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Biological effects of IR radiation:

Therapeutic applications (phototherapy)

Analgesic and spasmolytic effect (suppression of the pain) as a result of direct exposure of increased temperature and alternatively by the action on the skin receptors that induce reflex effects:

- joint pain in arthritis
- backbone (spine) syndromes
- neuralgia
- absorption of exudates in inflammatory processes (inflammation of the skin, sinusitis)
- reflective release of spasms during colic (kidney, gallbladder)



Sinusitis - the lack of the air transparency indicating fluid in contrast to the other side

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Biological effects of IR radiation:

Therapeutic applications (phototherapy)

IR lasers (thermal effect)

- Onychomycosis - treatment of fungal diseases of the nail plates (the basis of laser treatment is to heat the nail bed to a temperature of 40 to 60 °C to disrupt the growth of fungi).



- Acne treatment - heat destruction of the sebaceous glands.
- Rehabilitation (e.g. musculoskeletal system, Covid-19) - anti-inflammatory and biostimulation effect of radiation in the near IR area (penetrates through the tissues).

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