



# Medical treatment with phototherapy

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sense and simplicity



## Contents

<b>3</b>	Preface
<b>4</b>	The human being and sunlight in history
<b>6</b>	Light in prevention, therapy and rehabilitation
<b>12</b>	Side effects
<b>14</b>	Characteristics of optical radiation
<b>16</b>	Optical properties of the skin
<b>18</b>	Artificial light sources
<b>20</b>	Clinical references on usage of Philips UVB Narrowband (TL/01)
<b>24</b>	Pertinent references
<b>26</b>	Lamps and their applications

# Most effective on skin

For more than 100 years, Philips has been one of the pioneers in lighting. Today, as the world's largest manufacturer of lighting products, we employ a wealth of experience to satisfy lighting requirements for a multitude of applications. For photobiological and therapeutical purposes, Philips Lighting can provide a broad variety of lamps. Not only did we introduce the very first UVB lamps we've continued to develop and improve them for the last 20 years. Our application laboratory carries out research in close cooperation with universities and clinics throughout the world. Independent clinical studies have proven that Philips UVB narrowband phototherapy lamps are the most effective and safest for clinical use in the treatment for psoriasis, Vitiligo and other skin diseases\*. Based on this unmatched combination of experience and knowledge, Philips Lighting can offer the best advice to equipment manufacturers on any possible application.

Don't settle for poor imitations that could be harmful to patients. Insist on Philips. The only UVB narrowband phototherapy lamps that are certified to be the safest on skin.

## **Philips Lighting is the ideal partner**

This publication provides a review of the history and the current state of affairs regarding photomedical applications and a summary of the products now available.

There is always the possibility that new products emerge from the close cooperation between scientists and lamp manufacturers.

The more accurately the application, its action spectrum or the dosage is defined, the better the light source can be optimized as to its efficacy and economy.

\*Reference available at [www.philips.com/phototherapy](http://www.philips.com/phototherapy)

# The human being and sunlight in history

Far back in history, sun was considered a source of life. Indeed, it was often elevated to the status of a god and men believed in the healing powers of its rays. All over the world evidence has been found of cults worshipping sun-gods.

In ancient history the sun worship of the Pharaoh Akhenaton (1350 B.C.) was very important. He built temples dedicated to the light god, Aton. These temples were very unusual for the time as they had no roof, so the sunlight could freely fill the space inside. As an example to their co-religionists, Akhenaton and his family took off their clothes to benefit from the healing effects of the rays of the sun. The priests remained rather skeptical about this “enlightened” religion of Akhenaton. It flourished at the expense of their mystical and darker cults.

After the death of Akhenaton, the sun temples were soon pulled down. However, “sunbathing” continued to exist through the centuries in Egypt. The historian Herodotus (5th century B.C.) found this so remarkable that he described it in his chronicles: “The health-promoting properties of sunlight have been recognized from the beginning of civilization as a natural intuitive desire which causes humans, when in poor health, to be attracted by our largest optical radiation source: the sun.” In these early times, phototherapy (heliotherapy) was born and guided by experience rather than any scientific basis for the treatment of certain ailments. The Greek doctor and “father” of medical science Hippocrates (born in 460 B.C. on the island of Cos) had, on his many travels in Egypt, studied the sunlight treatment which was practiced there. On his return to Greece, he set up a clinic and medical school on the island of his birth thus breaking away from the medicine as practiced at the time by the priests. He was practicing medicine for the first time as a real empirical science. He wrote books on the surgery of fractures, hygiene and diets. In his sanatorium with its open gallery

facing south he treated patients on a scientific basis. He is, with good reason, considered to be the father of light therapy.

Later the Greeks and Romans continued this light therapy, otherwise known as heliotherapy. In the Roman baths (therms), famous throughout history, it was also possible to sunbathe in a solarium. The concept of the solarium dates from this time, indicating that use was being made of natural sunlight. Nowadays the word solarium refers to the use of an artificial sun, i.e. equipment containing special lamps. With the decline of the Roman Empire, heliotherapy disappeared. In the Dark Ages and with the spread of Christianity, medicine and hygiene declined, creating a situation where epidemics of cholera, plague and smallpox could easily break out. Also with the rise of Christianity, attention to the body and display of nakedness was considered sinful. All baths disappeared from houses and public bath houses were closed. The Swiss Arnold Rikli (1823-1906) reintroduced the positive effects of sunlight forgotten for many centuries, and used this effects as the basis of successful natural healing methods. He practiced for more than 50 years. He was responsible for developing therapeutic guidelines and ideas which are still valid today. His motto “Water is good, air is better and light is best of all” is at the core of heliotherapy. The Danish doctor Niels Ryberg Finsen (1860-1904) initiated an emphatic rebirth of light therapy in 1898. In that year he established a sun garden in Copenhagen (attached to the Finsen Institute) for his patients, where they could sunbathe completely naked. At the start, only natural sunlight was used, but because sunlight at this latitude (55°N) is not so plentiful, he soon

The sun can be regarded as an indispensable environmental factor in regulating our genetic material, biological rhythms and, in a broad sense, many photobiological processes via the skin and the eyes. What we know today about these photobiological processes is certainly only the tip of the iceberg.

changed over to the use of artificial light sources. Consequently he discovered that the ultraviolet part of the sunlight spectrum had a beneficial influence on the human body. In 1893 he demonstrated that red light was beneficial for healing the skin of smallpox patients. With artificially generated ultraviolet rays he could cure patients suffering from skin tuberculosis. In 1903, one year before his death, he received the Nobel Prize for Medicine.

It is clear that in the millions of years of evolution our bodies have become adapted and make use of the complete solar spectrum to regulate various body functions. The beneficial effects of ultraviolet rays were researched and valued much more in East European countries, such as Russia, than in the Western medical world. It is a great pity that in our Western society's attention is given almost exclusively to the negative effects of solar radiation. These negative acute and chronic effects only occur when the body is excessively exposed to this radiation. In general, no mention is made of the great benefits of UV radiation which can be received in full measure when it is used

in moderation. An important reason for this is that illnesses which were previously cured with the help of UV radiation are now treated with drugs including antibiotics. An example of this is skin tuberculosis (*lupus vulgaris*) which was formerly treated (discovered by Finsen) with UV radiation. This was later replaced by drugs and so treatment with ultraviolet radiation was quickly forgotten. With the present rapid increase in the use of medicines and the many objections which this has given rise to, the prophylactic and therapeutic effects of optical radiation deserve to receive much more attention.

In view of the long history of the relationship between man and the sun's rays, in this brochure written in a non-technical style, we are trying to create more interest in the positive effects of non-visual optical radiation. Since prehistoric times the evolution of all life on earth has taken place under the radiation of the sun.





# Light in prevention, therapy and rehabilitation

Nowadays, prevention, therapy and rehabilitation of certain diseases and conditions with optical radiation are the result of clinical studies guided by the progress in physics, chemistry and molecular biology. We have a greater understanding of the science behind what our ancestors did intuitively in previous centuries.



Picture by National Biological Corporation

Modern photomedicine started about 100 years ago with the already mentioned publication (1899) of Niels Finsen<sup>(1)</sup> in which he described the treatment of lupus vulgaris by ultraviolet radiation. At that time Finsen's results were attained by the rays of a strong carbon arc. Now, after 100 years of development, more sophisticated lamps are available for prophylactic and therapeutic purposes<sup>(2)</sup>.

## **Knowledge as the fundamental basis**

The past 30 years has seen an increase of publications concerning photobiological

research and photomedicine; this reflects the expanding potential of optical radiation for prevention and therapy. Of course, adequate knowledge and experience with handling optical radiation (ultraviolet, visible light and infrared) are essential if full advantage is to be taken of all potential uses. The aim is always to maximize the benefit whilst minimizing the level of risk. The correct dosage is the most important step. This means that phototherapy must always be carried out under the supervision of a doctor.

For more information view the video explaining Phototherapy treatment on our website [www.philips.com/phototherapy](http://www.philips.com/phototherapy)



# Ultraviolet

Here are the up to date aspects of UV "light" regarding prevention and therapy of various skin diseases.



Picture by Waldmann



Picture by Daavlin

## Light protection

It is one of the most important functions of the skin to build up its own light protection<sup>(3)</sup>. Melanogenesis and skin thickening can be activated by sunlight. However there is a possibility of sunburn, especially if there is an individual (genetic) disposition, such as in people with skin-types I to 4, (e.g. Caucasians). In this group the time to build up photo-protection needs to be extended with lower UV dosages. Thus the UV dosage must be in line with individual response and sensitivity according to skin-type. Sunlight has the highest intensities in the visible and near infrared region. The reflection in these regions is about 50% for all skintypes. This is also a natural protection mechanism. In calculating dosages one has to take this into account!

## Psoriasis

Psoriasis is a (primarily) genetically determined, multi-causal and chronic skin disease with wide spread red, raised skin lesions covered with silvery, white scales, which occurs worldwide, but is more prevalent in the temperate climatic zone. It affects 2% of all light-skinned people. It is a disease which is still incurable; moreover, no effective chemotherapy without side effects has yet been developed for treating such diseases. Photochemotherapy is one way of treating the disorder with a high success rate.

## PUVA photochemotherapy

A new era in therapeutic photomedicine was initiated at the start of the 1970's when, on the basis of research work carried out in USA and Austria, Parrish et al.<sup>(4)</sup>

described the systemic treatment of psoriasis by psoralens and irradiation with UVA, so-called PUVA therapy. At this time the concept of photochemotherapy was introduced. In photochemotherapy, the combination of a photosensitizing chemical compound and optical radiation is used to bring about a therapeutically beneficial result not produced by either the radiation or a drug alone. The drug may be applied topically or orally to reach the skin by blood circulation and is subsequently activated by irradiation with UVA. In practice, PUVA photochemotherapy is not only used for the treatment of psoriasis but for many other skin diseases as well (being in common use for more than 20 indications at present). It is applied by using a UV-sensitizing medicine and combining it with UVA lamps ('TL/09 and sometimes filtered HPA). The natural, UV-sensitizing psoralens (8 MOP, 5 MOP or others) are available in the market under various brand names. Recently it has been found that chronic and high dosage use of PUVA chemophototherapy in the treatment of psoriasis has serious negative side effects. Under the conditions indicated, the application of PUVA increases the risk of obtaining skin cancers including malignant melanoma. As a consequence there is a shift in preferred treatment protocols in favor of TL/01 phototherapy<sup>(5)</sup>.

## Broadband UVB/Narrowband UVB phototherapy

Phototherapy of psoriasis or other diseases of the skin is a type of therapy without any photo-sensitizing agent. It is the oldest form of treatment, and it is based on the experience with the favorable effects of sunlight on the general appearance of the skin. Numerous investigations show<sup>(6,7)</sup> that phototherapy with UVB is just as effective as PUVA therapy if the right doses are maintained. Another critical parameter is the UVB wavelength applied. Various investigations imply that the most favorable range for the effective UVB treatment of psoriasis is in the long-wave part of the UVB spectrum (between 305 and 315nm)<sup>(8,9)</sup>. This warrants a high (therapeutical) efficiency on the one hand and minimum (acute and chronic) risks on the other. There are mainly two types of fluorescent lamps of different spectral distribution - the TL/01-UVB Narrowband and the TL/12 UVB broadband lamp - available for the therapy of psoriasis. The erythral effect of the radiation from the TL/01 lamp is much smaller than from the TL/12 lamp so that - with the aim of being able to irradiate as much UVB as possible without producing erythema (reddening of the skin) - the TL/01 is a better proposition<sup>(8,9,10,11)</sup>. Moreover, recent investigations show that for successful therapy, TL/01 radiation can be dosed far below the erythral threshold<sup>(12)</sup>. This makes the period of exposure shorter, reducing overall dosages and thus any acute or chronic side-effects. TL/01 lamps have been tested world-wide in extensive clinical tests and are universally in practice. Irradiation equipment involving TL/01 lamps supply good means of home therapy as the dosage can

be easily controlled. The therapy schedule is drawn up by the doctor (adjustment of the individual sensitivity of the patient to the irradiation quality and quantity of the equipment) who will verify its success at regular intervals. Once the patient shows no symptoms any more a low-interval maintenance treatment is sometimes started to prevent early exacerbations.

Balneo-phototherapy the positive experience with the treatment of psoriatics at the Dead Sea is being increasingly transferred to the clinic. Brine baths, with a simultaneous or subsequent exposure to UVB (using TL/01) provide better results at a generally lower dosage than in UVB phototherapy. This is mainly attributed to the greater transparency of wet skin. Balneo-phototherapy of psoriasis is successfully applied for in-patients in numerous spas; it is also applied for outpatients in therapeutic centers<sup>(13)</sup>.

## Vitiligo

Vitiligo is a multi-causal disease, starting with the formation of a neoantigen, which triggers a cell mediated immune response leading to the destruction of melanocytes<sup>(14)</sup>. The depigmented lesions of skin and hair can be localized or generalized. It belongs to the group of the auto-immune disorders, e.g. Diabetes type I and thyroid disease, with which it is often associated. The prevalence is estimated at 0.5 to 1% worldwide, although in India a figure as high as 8% is reported. Skin diseases causing an altered or impaired appearance may profoundly affect those afflicted. Aside from causing physical discomfort and inconvenience, it has been demonstrated that they influence the patient's personal and social life, daily functioning

and psychologic status. Skin disease may provoke negative emotions such as shame or embarrassment, anxiety, lack of confidence and even psychiatric diseases like depression. The patients' self-image may be profoundly depressed and his self-esteem threatened. In the western world the quality of life (QOL) index scores in vitiligo patients are slightly lower than those of psoriasis patients. In the tropical region, where vitiligo was often confused with leprosy, patients with this disease are highly stigmatized. In India the QOL index scores of vitiligo patients supersede those of psoriasis patients<sup>(15)</sup>. Higher scores mean a lower quality of life. Unlike psoriasis, the possibilities for treating vitiligo are limited to phototherapy, except for a small number of patients with stable vitiligo, who can be treated with skin autologous pigment grafts. The first report of the use of "phototherapy" in the treatment of skin disorders dates from about 1400 BC among Hindus, as already mentioned. They used "photochemotherapy"-administration of plant extracts, followed by sun exposure-for vitiligo<sup>(2)</sup>. The same treatment was also used in ancient Egypt. The active ingredients in these plant extracts were isolated in 1947 by Fahmy et al.<sup>(16, 17, 18)</sup> as 8-methoxypsoralen (8-MOP) and 5-methoxypsoralen (5-MOP). In the same year, these authors and also El Mofty started to treat patients with vitiligo with 8-MOP and sun exposure<sup>(19)</sup>.

Kromayer, a German dermatologist, designed in 1904 a water cooled mercury vapor UV lamp<sup>(20)</sup>. He was the first to treat vitiligo with artificial UVB. In 1969 Fulton et al.<sup>(21)</sup> used "black light" UVA tubes for the first time in combination with topical 8-MOP in the treatment of vitiligo. Parrish and Fitzpatrick



introduced modern photochemotherapy with 8-MOP, having a peak sensitivity at 330 nm and UVA fluorescent tubes. They used fluorescent tubes emitting in the 320 - 380 nm waveband in the PUVA treatment of vitiligo<sup>(22)</sup>. Although late effects, e.g. skin carcinogenesis, have rarely been reported in vitiligo, the frequently observed phototoxic responses were considered a severe practical problem. Narrowband (NB)-UVB, or 311 nm UVB (Philips TL 01) has been used in the treatment of vitiligo now for 10 years and was first reported by Westerhof and Nieuweboer-Krobotova<sup>(23)</sup>. It is now considered as the treatment of choice, because of its advantages over PUVA treatment being: UVB 311 nm is more effective than PUVA and safer, as there are no psoralen-induced side effects and can be used in children and pregnant woman. The NB-UVB can also be achieved with the excimer laser (308 nm)<sup>(24)</sup>. A drawback is that only small areas can be treated at one time and the excimer laser is excluded from home treatment. Narrowband UVB is also recommended in combination with pigment cell grafting of vitiligo lesions<sup>(25)</sup>.

#### Atopic dermatitis

Atopic dermatitis (atopic eczema, neuro-dermatitis) is a constitutional, inflammatory, pruritic skin disease, usually progressing chronically. The therapy of AD includes mainly corticosteroids (CS), antihistamines and immunosuppressors. CS are known to cause a variety of side effects and attempts have been made to reduce or eliminate their use through alternative methods such as phototherapy (UVA/UVB, UVA(1), UVA(2), UVB 311 nm). In the majority of patients, UV irradiation proves favorable<sup>(26)</sup>. The active spectrum is mostly in the UV range,

between 300 and 400 nm (equipment with TL/10 (=UVA-2), 'TL'/09, filtered HPA). The dosage (quality and quantity of radiation) has to be adjusted to the individual response of the patient and possibly (in case of a reaction of adaptation) be altered in the course of the therapy. 311 nm UVB therapies has been found to be ideal for following UVA-I therapy: UVA-I is used in the initial phase of treatment to manage acute, severe exacerbations of atopic dermatitis<sup>(5)</sup> and is replaced by 311 nm UVB therapy, which is an effective (and presumably safe) means of maintenance therapy. Because its presumed safety, it has also been advocated to be used for children<sup>(27)</sup>.

#### Other skin diseases

Psoriasis, which affects about 2% of Caucasians, and vitiligo, which affects a similar percentage of the dark and light-skinned population, are two examples of skin diseases which can be successfully treated with phototherapy. But the list of skin diseases which can be treated with photochemotherapy is constantly growing. Some other dermatoses responsive to photochemotherapy are parapsoriasis, cutaneous T-cell lymphoma (Sézary syndrome), mycosis fungoides, lichen planus, pityriasis lichenoides, pityriasis rosea, various types of eczema, polymorphous light eruption, furunculosis, folliculitis, indolent ulcers, prurigo and pruritis, etc. Most of these diseases have now been treated with Narrowband UVB, although in a varying degree of effectiveness, which seem to be as good as PUVA<sup>(28)</sup>. It has also been stated that exposure to ultraviolet "light" causes an exacerbation or produces injurious effects in the following conditions: xeroderma

pigmentosum, herpes simplex, lupus erythematosus, several types of eczema, prematurely senile skin, porphyria, the use of immunosuppressive medications (after kidney transplants) and Aids.

#### Vitamin D photosynthesis

By means of UV irradiation, the provitamin D7 (7-dehydrocholesterol) is transformed into pre-vitamin in the outer skin. In the process of hydroxylation in the liver and the kidneys, the bio-active form of vitamin D3 is formed, controlling the calcium metabolism and being hormonal in type. Above all, vitamin D3 influences cellular information, cell differentiation, endocrine regulatory systems, immune reactions, macrophage functions as well as the myocardial metabolism. It has a practical use in preventing rachitis, osteoporosis, osteomalacia, cancer of the colon, prostate cancer and breast cancer<sup>(29,30,31,32)</sup>. The active spectrum of UV inducing vitamin D is limited to the UV range below 320 nm. Dosages are much lower than those causing sun-burn (equipment with TL/01, HPA filtered).



Picture by Waldmann

# Light

The visible range of optical radiation is now also used in prevention and therapy of a number of diseases and conditions.

- Phototherapy for hyperbilirubinemia
- Phototherapy for winter depression (SAD), the jetlag syndrome and the shift-worker syndrome
- Photodynamic therapy with red light of skin precancer and certain superficial types of skin cancer
- Prevention and rehabilitation (practiced by physiotherapists)



Picture by Sigma

## Acne

Acne vulgaris is a chronic skin disorder chiefly found in adolescents, caused by inflammation (induced by propionibacterium acnes) of the skin glands and hair follicles mainly of the face, chest and shoulders. All types of radiation may be applicable and lead to improvement: UVB and UVA radiation as well as intensive visible radiation (light in the blue and green wavelength range with 'TL'/03, 'TL'/52, TL'/17 or filtered metal iodide lamps which are doped with indium or gallium), depending on the type of acne and the reaction of the individual patient<sup>(33)</sup>. Recently good results have been reported about the combination of blue (415 nm) and red (660 nm) light using low-intensity fluorescent lamps<sup>(34)</sup>. These phototherapeutic approaches have no side effects and are therefore preferred above other medical (drug) treatments<sup>(35)</sup>.

## Hyperbilirubinemia (neonatal jaundice)

An example of phototherapy in the visible region is the treatment of hyperbilirubinemia with blue light (400-500 nm). Unconjugated bilirubin, being a decomposition product of haemoglobin, is not fully soluble in water and plasma. In normal physiological circumstances, this unconjugated bilirubin is bound to albumin and transported to the liver where it is converted by glucuronyltransferase into the water-soluble conjugated form and excreted in the bile. When the albumin binding capacity of the plasma is exceeded (e.g. in icterus neonatorum, in Crigler Najjar syndrome, etc), the unconjugated bilirubin can diffuse into the tissues. Blue light can convert this unconjugated form into a more watersoluble form by a photo-oxidative process and an isomerization process<sup>(36)</sup>. Figure 7 (page 19)

illustrates the spectrum of a blue lamp TL/52, just emitting at the maximum effective wavelength of 450 nm. The blue light component in halogen dichroic mirror lamps can also be used (UV and IR filtering is necessary). There has also been research showing the bilirubin content of the plasma being lowered with the help of green light ('TL'/50). However, the results are still not convincing enough to warrant a change from blue light. The effective use of phototherapy has eliminated the need for exchange transfusion in almost all jaundiced infants. Care must be taken to ensure effective irradiance delivery, to maximize skin exposure and to provide eye protection.

## Photodynamic therapy

Photodynamic therapy (PDT) is a two-step therapeutic technique in which the topical or systemic delivery of photosensitizing drugs is followed by irradiation with visible light. Activated photosensitizers transfer energy to molecular oxygen, generating reactive oxygen species (ROS). The subsequent oxidation of lipids, amino acids and proteins induces cell necrosis and apoptosis. In addition, ROS indirectly stimulate the transcription and release of inflammatory mediators. The photosensitizers are selective, in that they penetrate and accumulate in tumor cells or in the endothelium of newly formed vessels while generally avoiding the surrounding healthy tissue. The mechanisms of penetration through the cell membrane and the pattern of subcellular localization strongly influence the type of cellular effect. The technique is simple and effective: the topical application of aminolaevulinic acid (ALA) and its methyl ester (methyl aminolaevulinate, MAL) followed by irradiation with broadband

red light in the 630 nm range<sup>(30)</sup>. Further promising photosensitising drugs for use in photodynamic therapy will most probably be the phthalocyanines with a high extinction coefficient between 650 and 780 nm, still in the range of the optical window (cf. also “Optical characteristics of the skin”)<sup>(37)</sup>. In several randomized, controlled studies, the application of a standard preparation containing MAL, followed by red light irradiation proved effective and well tolerated in the treatment of actinic keratosis and basal cell carcinoma, and has now been approved for clinical use in European countries. A brand name aminolevulinic acid solution plus blue light exposure has been approved for the treatment of actinic keratosis in the USA. Randomized and controlled studies have shown that MAL as well as ALA are also effective in the treatment of Bowen’s disease<sup>(38)</sup>. Appropriate radiation sources are f.i. filtered MSR-lamps or special fluorescent lamps with a radiation maximum around 630 nm.

#### SAD - seasonal affective disorder

Light therapy can also be used in a totally different field: in the so-called seasonal affective disorder (SAD) syndrome. The application of bright light (>2500 lux and high colour temperature) is an effective treatment for winter depression. It has been postulated that since bright light is capable of suppressing the hormone melatonin, this hormone moderates the effects of shortening days on symptoms of SAD in wintertime<sup>(39,40)</sup>. For this type of phototherapy, we recommend the fluorescent lamp TLD/930, 940, 950 “natural daylight.” Consideration must be given not only to luminance (illuminance is a useful parameter) but also to other parameters (e.g. size of the radiated area on the retina)

as well as safety aspects for equipment design. There are also indications that this therapy is successful for treating jetlag and the shift-worker syndrome.

#### Further effects

In general, suberythemal doses of UVB “light” have many bio-positive systemic effects on the human being, which can be used in prevention, in sports physiotherapy (e.g. muscle sprains and tendonitis) and in the rehabilitation of patients. Some of these effects are as follows: Vitamin-D synthesis in skin (prevention of rachitis, osteoporosis, etc.), reduction of blood pressure<sup>(41)</sup>. In many cases, these effects can be obtained from radiation with low doses - equipment with a small amount of UVB in a solarium, thus compensating for a possible shortage during the darker months with less sun (September to April).



Picture by Jelosil



Philips EnergyLight



# Side effects

Since the late 1980's PUVA therapy has been largely replaced by Narrowband UVB due to the many side effects<sup>(42,43)</sup>.



## UVA (PUVA)

Short-term side effects when using PUVA to treat psoriasis include:

- Skin redness, headache, nausea, itching, burns
- Disturbed liver functions
- The spread of psoriasis to skin that was not affected before
- Nausea from the medication
- Squamous cell carcinoma or melanoma

Long-term side effects when using PUVA to treat psoriasis include:

- Premature skin damage associated with sun exposure
- Hypertrichosis
- Discolored spots on the skin
- Actinic keratosis
- Nonmelanoma skin cancer
- Cataracts (Cataracts may be avoided by wearing goggles during treatments and UV blocking sunglasses outdoors for the first 24 hours after treatment)
- Weakened immune system

Psoralens should not be used by:

- Children under age 12
- People who have diseases that make their skin more sensitive to sunlight (such as lupus)
- Fertile men and women who do not use birth control
- Pregnant women, because of possible effects on developing fetuses
- In male patients the genitals should be covered due to increased risk of skin cancer

## UVB broadband

Early side effects of UVB broadband are erythema and skin dryness. The maximum erythema occurs 8-24 hours after irradiation. The therapeutic effectiveness of UVB broadband is the highest close to erythemogenic doses. This means that erythema is likely to occur<sup>(9)</sup>.

Chronic exposure to UV causes premature aging of the skin. No evidence yet on differences between the effect of UVA, UVB broadband and UVB Narrowband on skin aging. In contrast to the undisputed role of PUVA in skin tumor induction, no significant increase in the risk of developing squamous cell carcinoma or basal cell carcinoma has been associated with long term exposure to UVB even in combination with coal tar over 25 years<sup>(9)</sup>.

When used in humans, Narrowband UVB seems not have a difference in the carcinogenic risk compared to broadband UVB, but they both have a clear significant lower risk compared to PUVA therapy. A 10 year follow up study of patient exposed to UVB broadband or Narrowband showed no significantly increase in the risk of skin cancer<sup>(35)</sup>.

## UVB Narrowband Blue light

Early side effects of UVB Narrowband are erythema and skin dryness. The maximum erythema occurs 8-24 hours after irradiation. However compared to broadband UVB Narrowband UVB has been shown to be effective at the sub-erythemogenic doses. Therefore, erythema and DNA damage is less likely to occur with UVB Narrowband phototherapy<sup>(11)</sup>. Chronic exposure to UV causes premature aging of the skin. No evidence yet on differences between the effect of UVA, UVB broadband and UVB Narrowband on skin aging.

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When used in humans, Narrowband UVB seems not have a difference in the carcinogenic risk compared to broadband UVB, but they both have a clear significant lower risk compared to PUVA therapy. A 10 year follow up study of patient exposed to UVB broadband or Narrowband showed no significant increase in the risk of skin cancer<sup>(44)</sup>.

Blue light hazard is defined as the potential for a photochemical induced retinal injury resulting from radiation exposure at wavelengths primarily between 400 nm and 500 nm<sup>(45)</sup>.

For the purposes of this discussion, blue light is defined as light within the wavelength range of 400-480 nm, because over 88% of the risk of photo-oxidative damage to the retina from fluorescent lamps (cool white or 'broad spectrum') is due to light wavelengths in the range of 400-480 nm. The blue light hazard peaks at 440 nm, and falls to 80% of peak at 460 and 415 nm. In contrast, green light of 500 nm is only one-tenth as hazardous to the retina than blue light with a wavelength of 440 nm<sup>(46)</sup>.

The mechanisms for photochemical induced retinal injury are caused by the absorption of light by photoreceptors in the eye. Under normal conditions when light hits a photoreceptor, the cell bleaches and becomes useless until it has recovered through a metabolic process called the "visual cycle"<sup>(47,48,49)</sup>. Absorption of blue light, however, has been shown to cause a reversal of the process where cells become unbleached and responsive again to light before it is ready. This greatly increases the potential for oxidative damage<sup>(50)</sup>. By this mechanism, some biological tissues such as skin, the lens of the eye, and in particular the retina may show irreversible changes induced by prolonged exposure to moderate levels of UV radiation and short-wavelength light. According to some of these studies, blue light waves may be especially toxic to those of us who are prone to macular problems due to genetics, nutrition, environment, health habits, and aging<sup>(50,51,52)</sup>.

# Characteristics of optical radiation

The spectrum of optical radiation (Fig. 1) lies between 100 nm (in the UV range) and 1 mm (in the IR range). For practical purposes, this wavelength range is subdivided into seven bands in accordance with CIE (International Commission on Illumination)

UVC from 100 to 280 nm (short-wave UV)

UVB from 280 to 315 nm (medium-wave UV)

UVA from 315 to 380(400) nm (long-wave UV)

Light (visible radiation) from 380(400) to 780 nm

IR-A from 780 to 1400 nm (short-wave infrared radiation)

IR-B from 1.4 to 3  $\mu\text{m}$  (medium-wave infrared radiation)

IR-C from 3  $\mu\text{m}$  to 1 mm (long-wave infrared radiation).

Not only ultraviolet “light” but also visible and

infrared “light” have many possible applications in photobiology and photomedicine.

Ultraviolet, visible and infrared radiation has distinctive physical, photobiological and photochemical features. Going from the infrared towards the ultraviolet region, the energy content (photon energy) of the “light” increases. Most photobiological effects in the ultraviolet and visible region are due to photochemical reactions, whereas effects in the infrared region are mostly due to heat dissipation.

Photochemical reactions are controlled by several basic laws of which the most important

are the following: According to the Draper-Grotthus law, interaction between “light” and matter can only occur if the “light” is absorbed by the matter involved. If this is not the case, then the radiation will be reflected or transmitted or scattered. The second law known as the Bunsen-Roscoe law or reciprocity law states that the quantity of the reaction products of a photochemical reaction is proportional to the product of the irradiance of the “light” and the exposure time. This product is called the dose.

Also in photobiology the effect depends on the dose rather than the intensity of the light. The same dose (with the same effect) can be provided by a high intensity in a short time or a low intensity in a long time. So if “light” is absorbed by, for example, the skin, the resulting effect is dependent on the exposure dose rather than the irradiance level. In photobiology this is called the “dose-response” relation for a particular effect. As stated before, optical radiation can only be effective if absorbed by so called chromophores within the matter involved. These chromophores can be biological molecules like DNA, RNA, proteins or drugs. The absorbed ultraviolet or visible “light” can break or change a chemical bond in a molecule, or create bonds between two or more molecules. Absorbed infrared radiation excites rotational or vibrational energy levels in a molecule, causing a photophysical reaction. This absorption leads to heat dissipation in the absorbing matter. This warming effect is used in many medical applications like thermotherapy, hyperthermia and in sports physiotherapy. However, it can also be an unwanted side effect (depending on the wavelength).

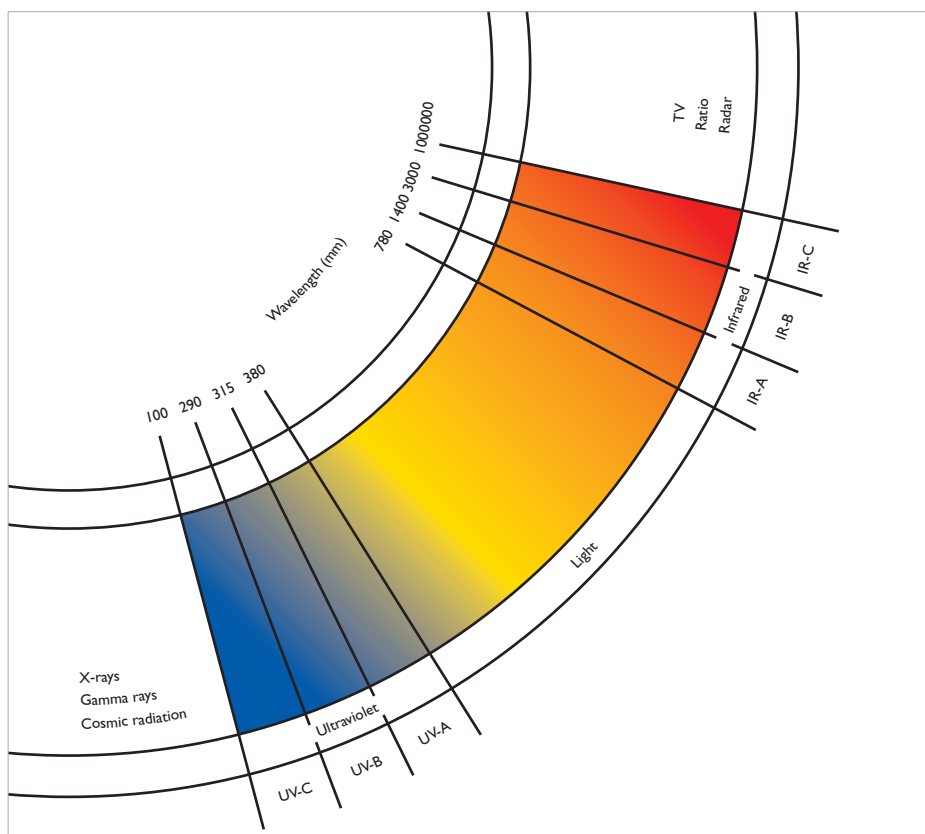


Fig. 1 Spectrum of the sun





# Optical properties of the skin

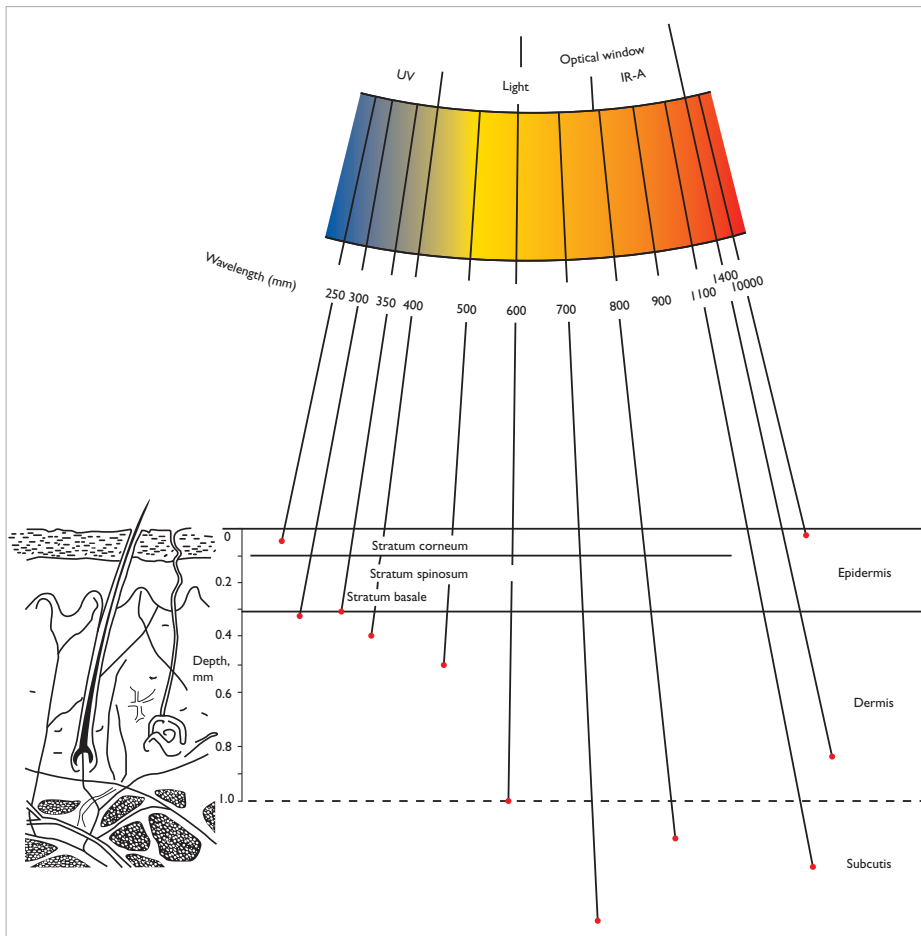


Fig. 2 Skin penetration depth of optical radiation

Knowledge of the optical properties of the skin is indispensable for understanding the effects of optical radiation.

Optically, the skin can be regarded as an inhomogeneous medium consisting of four layers:

- Stratum corneum
- Stratum spinosum, } Epidermis (50 - 150µm thick) incl. stratum basale
- Dermis (0.8 - 1 mm)
- Subcutis (1 - 3 mm)

These layers have different refractive indices and distributions of chromophores, which will bring about different reflecting, transmission and scattering characteristics depending on the wavelength. Figure 2 gives a schematic representation of the skin layers and the depth of penetration as a function of the wavelength. The reflection of radiation in the 250-300 nm regions both against and in the stratum corneum is about 4-7%. Towards the longer wavelength the reflection of the skin increases. At about 800 nm there is a maximum reflection of 40-60% depending on the skin type. Going further towards the IR the reflection decreases to an average value of 5-10% in the IR-B region.

The degree of reflection is also dependent on the melanin content; the darker the skin, the less the radiation will be reflected, especially in the visible region. Refraction of the radiation is mostly the result of the structure of the stratum corneum, while scattering is the result of interaction between the light and the particles according to the wavelength of the light. The attenuation of radiation in the epidermis is primarily due to absorption by chromophores and, secondly, by scattering. The chromophores in the stratum corneum are predominantly melanin, urocanic acid



and proteins consisting of aromatic amino acids like tyrosine and tryptophan. The stratum malpighi, (= stratum basale plus stratum spinosum), consisting of viable cells (keratinocytes), has the same chromophores as the stratum corneum, but here the nucleic acids of DNA and RNA play an important role in absorbing short-wave UV. The absorption behavior and reaction of the skin to UV exposure differs considerably depending on the particular individual. Six skin types (four light-skin, two dark-skin types) have been defined in a commonly used international classification based on erythema formation and pigmentation capability of the skin when exposed to sunlight. The penetration of “light” into the dermis, because of the vascularization, is also influenced by the radiation absorbance of the blood (haemoglobin and oxyhemoglobin) in the 400-600 nm region and by the scattering of light by collagen fibers. In Figure 2 it can be seen that the greater part of UVC is absorbed in the stratum corneum (90%) and that 90% of the UVB is absorbed in the epidermis but that a considerable part of the UVA can reach the dermis which contains blood vessels. The thin epidermis has no blood vessels of its own, but receives what it needs from the capillary blood vessels immediately below the basal-cell layer of the epidermis. Light with a wavelength between 600 and 1400 nm (red light, short-wave infrared) can penetrate into the subcutis and is therefore called the “optical window” of the skin.



# Artificial light sources

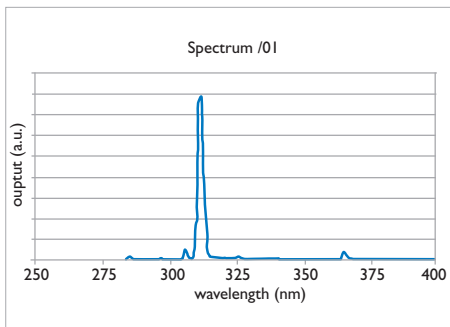


Fig. 3

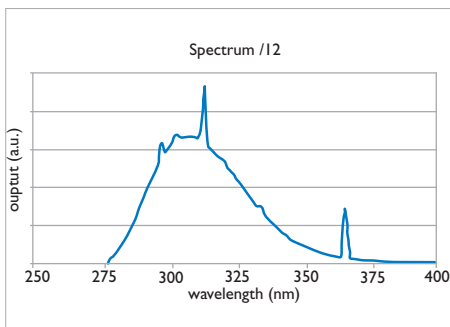


Fig. 4

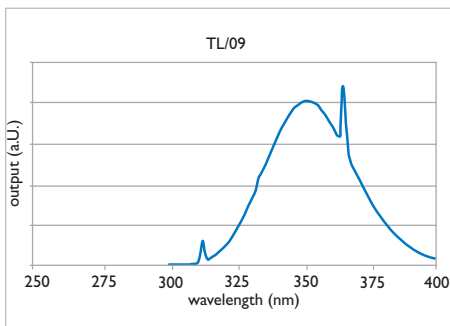


Fig. 5

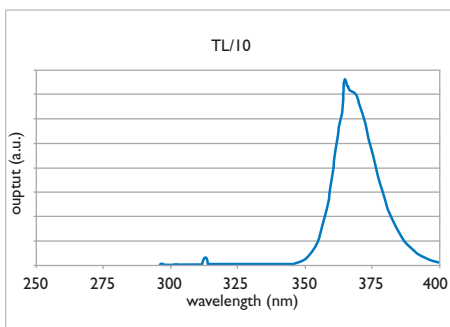


Fig. 6

Artificial light sources can be divided into the following groups:

Incandescent lamps:

- Normal lamps
- Halogen lamps
- Infrared lamps

Gas-discharge lamps:

- Low-pressure lamps
- Medium-pressure lamps
- High-pressure lamps

Although lasers, LEDs (light-emitting diodes) and LCDs (liquid crystal displays) also belong to the group of sources producing optical radiation, they will not be described in this brochure since their technology and application are totally different from those of "lamps". The basic principles of lamps will be briefly explained in the following (for detailed technical information concerning light and radiation sources and optimum application thereof in equipment, please contact Philips Lighting, addresses at the back of this brochure.

## Ultraviolet

### Gas-discharge lamps

A gas-discharge lamp is based on an electrical discharge through a gas or vapor. In most cases the discharge is sustained by the ionization of mercury vapor or, in other cases, by inert gases like Xe, Ar and Ne. Depending on the mercury vapor pressure these lamps can be divided into:

- Low-pressure
- Medium-pressure
- High-pressure

The emitted spectrum of these lamps changes from low- to high-pressure due to the increased population of the higher energy

levels of mercury. In consequence, the emitted energy distribution is shifted from the high photon energy lines (185 and 254 nm) towards the lower photon energy lines, i.e. towards the UVA range and the visible part of the spectrum. With the increasing mercury pressure we also get a broadening of the emission lines due to the influence of atoms or ions close to the excited atom during its emission of radiation.

### Low-pressure mercury lamps

(with special transmission glass and without fluorescent layer). Tubular germicidal lamps ("TUV") belong to the group of the low-pressure lamps. The germicidal "TUV" lamp (Fig. 3) emits about 95% of its energy in the 254 nm mercury line. The action spectrum for inactivation of micro-organisms has its maximum at about 265 nm (DNA absorption) and therefore this lamp type is mostly used for sterilization and disinfection. Many of these lamps are used, as an alternative to chlorine, for the disinfection of drinking water and waste water. Also, air contamination in operating theatres (for longer operations) can nowadays be reduced to well below the suggested upper limit for ultra clean air systems ( $10 \text{ cfu/m}_3$ ) by combining the use of "TUV" lamps (UVC) and occlusive working clothes, which is a very cheap solution to the problem.

### Fluorescent lamps

Fluorescent lamps ('TL') are also low-pressure mercury lamps with a fluorescent layer on the inside of the glass envelope which transforms the short-wave ultraviolet energy of the gas-discharge into useful radiation depending on the type of phosphorus. It is well known that for illuminating purposes many types of phosphorus are available. In the UVB region, the 'TL/01' and 'TL/12' lamps are used in

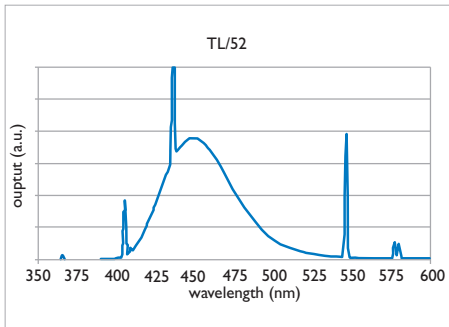


Fig. 7

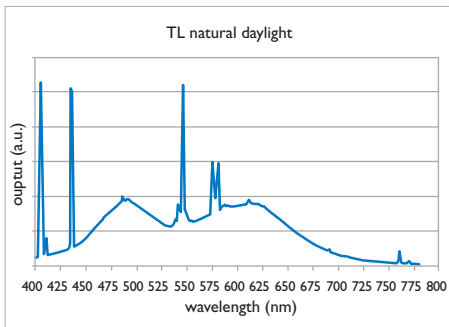


Fig. 8

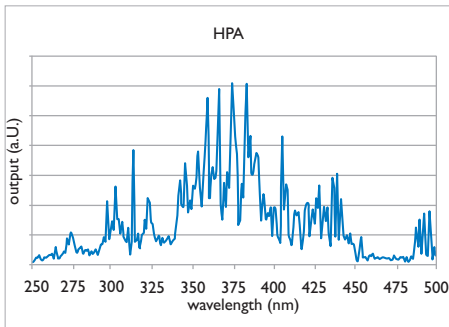


Fig. 9

phototherapy and the spectra are presented in Figures 3 and 4, respectively. In the UVA range, three lamps are available with a maximum emission at 350 nm ('TL'/09) and at 370 nm ('TL'/10). These lamps are primarily used in photochemotherapy but also in phototherapy, e.g. for neurodermatitis. The spectra are presented in Figures 5 and 6, respectively. The later two lamps are also available with built-in reflectors coded as 'TL'/10R, 'TL'/09R. Since an external reflector has now become unnecessary, the lamps can be mounted closer together in order to increase the irradiance level (up to two-fold increase in comparison with systems with an external reflector) and consequently provide shorter treatment times. Note: The lamp type designations may change - please request up-to-date information.

## Light

In the visible region, other lamps used in the phototherapy of hyperbilirubinemia must be mentioned: the 'TL'/52 with the maximum wavelength at 450 nm (Fig. 7). For the treatment of seasonal affective disorder (SAD), we strongly recommend the use of the so called 'Bright light' lamps (Fig. 8) with 6500K color temperature ("Natural Daylight"), preferably in combination with high-frequency electronic gear.

### Metal-halide lamps

In medium-pressure lamps with additives like iron and cobalt halides, the emission is due to the excitation of these additives rather than the mercury. These HPA lamps (Fig. 9) are provided with special filters, and are used in phototherapy and photochemotherapy (usually with additional filtering. Virtually any spectrum can be enhanced by the addition of various

metal halides, in the UV as well as in the visible range (MSR, HPI, etc.)

### Filtering

Because of their fluorescing abilities, UVA gas-discharge lamps with Wood's glass envelopes - so-called "blacklight blue" lamps (types "HPW", "MLW" and 'TL'/08) - which emit only UV in the 365 nm region (without visible light) can play an important role in the diagnosis of skin diseases like tinea capitis, pityriasis alba and vitiligo. These lamps are also used in the treatment of, for example, palmar psoriasis and alopecia areata. Whereas fluorescent lamps usually do not have to be filtered additionally in order to eliminate unwanted radiation components, this is still frequently necessary with medium-pressure and high-pressure lamps, depending on the specific application and requirements relating to the desired spectrum. The filters have to meet high demands (incl. temperature resistance, low spectral transmission scatter, high spectral stability throughout service life).

### Equipment design

As the radiation is used primarily for treating surfaces, the radiation energy produced in the lamps must be directed by means of reflectors. The desired spectrum, necessary intensity, area to be treated, size and angle of incidence determine the type and quantity of the radiation source, the form and material of the reflector and the choice of filter. The lamps must always be operated under the operating conditions specified by the lamp manufacturer (cooling, ballasts, etc.). Safety regulations and official instructions as well as workplace protection requirements must be observed when UV lamps are used (these differ from country to country).

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# Lamps and their applications

Indications in the ultraviolet region	Wavelength region (nm)	Wavelength max (nm)	Philips-Radiation sources
<b>Effects on/via skin</b>			
Building up sun protection	280-380	300	
Vitiligo, phototherapy of	280-350	310, UVB	TL/01, TL/12
Polymorphous light eruption, conditioning of	280-380	315	TL/09, TL/01, TL/12
Psoriasis phototherapy (SUP)	300-320	311	TL/01, TL/12
Acne phototherapy	300-400	UVA, UVB	
Atopic eczema, phototherapy of	300-400	individual/variable	TL/10 (filtered), TL/09, TL/01
PUVA photochemotherapy (psoriasis and others)	320-380	330....350	TL/09
Photopheresis	250-400	330....350	TL/08, TL/09
Photoreactivation	350-480		TL/10, (TL/52)
UV-blood irradiation	UVC, UVB, UVA, Blue light	254, 306, 370, 460	PL-TUV, PL/12, PL/10, PL/52
<b>Application in physical medicine</b>			
Photosynthesis of vitamin D3	255-320	295	TL/01
Phagocytosis, improvement in	300-380	350	TL/09
Hearth/cardiovascular system, positive stimulation of	300-400	300	TL/109
Blood fluidity, improvement of	300-380	350	TL/09
Cholesterol, lowering of	320-400	370	TL/09, TL/10
Blood irradiation	UVC, UVB, UVA, Blue light	254, 306, 370, 460	PL-TUV, /12, /10, /52

Indications in the visible region (light)	Wavelength region (nm)	Wavelength max (nm)	Philips-Radiation sources
<b>Effects via the eyes/via the skin</b>			
SAD-Seasonal effective disorder (also jetlag, shiftworker syndrome, PMS syndrome); improvement vigilance and activity; influence on circadian rhythm	400 - 780 (without UV)	continuous	TL/96, /95 'Nat.daylight' /HF-operation TL/840, 850 (R) /HF-operation
Helio phototherapy (eyes, skin)	light	continuous	MSR-lamps (filtered)
<b>Effects via/on the skin</b>			
Photoreactivation	350 - 480	±400	TL/52 (TL/10)
Newborn icterus, phototherapy	420 - 520	460	TL/52, PL/52
Acne-phototherapy (propioni bact.)	blue, green		TL spec.
PDT-photodynamic therapy	600 - 800	630 (and others)	HID-red (= f (Sensibil.), MSR)
Helio-phototherapy (eyes, skin)	UV + light + UR	continuous	MSR lamps (filtered)





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