

# Physicochemical properties of selected compounds used as ultraviolet filters in cosmetics

## Właściwości fizykochemiczne wybranych związków stosowanych jako filtry ultrafioletowe w kosmetykach

### ABSTRACT

An ultraviolet filter is defined as a substance, mixture, or material that blocks or absorbs radiation in the UV range, and its key purpose is to protect the skin from the harmful effects of radiation. Consumer concern is mainly regarding organic filters and the frequent problems with their low photostability, which is highly undesirable in terms of safety.

The aim of this work was to discuss the term “photostability” and to assess the safety of the three most popular compounds classified as ultraviolet filters. Cited studies and issued opinions by Scientific Committees on Customer Safety confirm the safety for human health of Avobenzone, Oxybenzone and Octinoxate in strictly defined maximum concentrations.

Side effects of these filters, like accumulation in the bloodstream, may occur after prolonged use. In order to improve the level of photostability of Avobenzone and Octinoxate the following methods are used: the use of photostabilizers and excited state quenchers, encapsulation of the molecule in micelles or the addition of antioxidants such as vitamin C. Although these compounds do not pose a serious threat to human health, two of them (Oxybenzone and Octinoxate) have a negative impact on aquatic ecosystems.

**Keywords:** UV filters, organic filters, *Avobenzone*, *Oxybenzone*, *Octinoxate*

### STRESZCZENIE

Filtr ultrafioletowy definiowany jest jako substancja, mieszanina lub materiał, który blokuje lub absorbuje promieniowanie w zakresie UV, a jego głównym zadaniem jest ochrona skóry przed szkodliwym działaniem promieniowania. Obawę konsumentów przed niepełną ochroną budzą głównie filtry organiczne i ich niska fotostabilność, która jest wielce niepożądana w kwestii bezpieczeństwa użytkowania.

Celem pracy było odpowiednie zdefiniowanie terminu fotostabilność oraz ocena bezpieczeństwa stosowania 3 najpopularniejszych związków klasyfikowanych jako filtry ultrafioletowe. Przytoczone badania oraz opinie wydane przez *Scientific Committee on Customer Safety* potwierdzają bezpieczeństwo stosowania dla zdrowia człowieka Avobenzone, Oxybenzone i Octinoxate w ściśle określonych stężeniach maksymalnych.

Skutki uboczne stosowania tych filtrów, np. akumulacja w krwiobiegu, mogą się pojawić po dłuższym czasie stosowania. Aby poprawić poziom fotostabilności Avobenzone oraz Octinoxate, stosuje się następujące zabiegi: stosowanie fotostabilizatorów oraz wygaszaczy stanów wzbudzonych, zamykanie cząsteczek w micelach czy dodatek antyoksydantów np. witaminy C. Mimo że związki te nie stanowią poważnego zagrożenia dla zdrowia człowieka, dwa z nich (Oxybenzone i Octinoxate) mają negatywny wpływ na ekosystemy wodne.

**Słowa kluczowe:** filtry ultrafioletowe, UV, filtry organiczne, *Avobenzone*, *Oxybenzone*, *Octinoxate*

## INTRODUCTION

The main task of UV-protective substances used in cosmetics is to protect the skin against the negative effects of ultraviolet radiation (UV), alleviate the photoaging processes, limit the formation of wrinkles and discolorations, and to reduce collagen loss [1]. Efficient products should protect against both UVA and UVB (UVA to UVB protection ratio not smaller than 1:3), which means the filter mixture should cover the entire spectrum of ultraviolet radiation. The effectiveness depends on the range of blocked/absorbed radiation, a level of the sun protective factor (SPF) and UVA (PPD, persistent pigment darkening). The recommended amount of sunscreen is 2 mg/cm<sup>2</sup> of the skin surface [2].

There are two types of filters that differ in their mechanism of action: physical filters (also known as inorganic filters), and chemical filters, (so-called organic filters). Inorganic filters reflect from the surface of the skin and scatter UV photons, protecting against UVA, UVB, and some parts of visible radiation. Organic filters are responsible for absorbing radiation and converting absorbed energy into heat, but they do not equally absorb radiation from both UVA and UVB ranges.

The aim of the study was to present the most important information about the structures, physicochemical properties, and photostability of selected organic UV filters, as well as to discuss the safety problems with their usage.

## TYPES OF RADIATION AND THEIR EFFECTS ON THE SKIN

There are three types of electromagnetic radiation: ultraviolet, visible, and infrared [3]. Ultraviolet radiation covers the wavelength in the range of 100-400 nm. It consists of UVA, UVB and UVC radiation depending on wavelength and degree of absorption by the Earth's ozone layer.

### UVA radiation

The wavelength of UVA is 315-400 nm and almost entirely reach the surface of the Earth [4]. For this reason, exposure to its negative effects is the same throughout the year. Moreover, it passes through windowpanes. Since this type of radiation penetrates the deepest layers of the skin, it causes an immediate tan effect. In addition, it significantly affects the skin aging processes and accelerates wrinkles formation, by reducing the skin's ability to bind water and release collagenase from fibroblasts, which is an enzyme that causes the breakdown of collagen fibres UVA also affects the development of skin cancers because it intensifies the process of uncontrolled cell division and the formation of free radicals, which are one of the causes of cell DNA damage [2, 5]. In addition, this type of UV radiation affects immunocompetent cells and vascular endothelium [1].

### UVB radiation

UVB is radiation in the range of 280-315 nm. It is partially absorbed by the ozone layer and does not penetrate through

windowpanes or clouds. It is biologically active, although it does not pass beyond the surface of the skin. Since no more than 10% of this radiation reaches the surface of the Earth, the tan and burns are formed with a delay. Despite this, it intensifies the aging process and the development of skin cancer [1, 3, 5].

### UVC radiation

UVC, radiation in the range of 100-280 nm, is completely blocked by the ozone layer in the atmosphere, therefore the only sources of UVC are artificial and man-made (e.g. bactericidal fluorescent lamps). UVC radiation is deadly for living organisms, but it is also characterized by a very low degree of penetration and practically does not penetrate the epidermis. Due to the above, it is not considered when developing UV-protective cosmetics.

## MECHANISMS OF UV RADIATION SUPPRESSION

There are two ways of interacting electromagnetic radiation with matter – absorption and scattering. In sunscreens (especially in inorganic filters), both mechanisms are equally important [6].

When the photon is absorbed by an organic filter molecule, electrons from the HOMO, the highest occupied molecular orbital, are transferred to the lowest unoccupied molecular orbital (LUMO) (Fig. 1). The excited state can be deactivated in several different ways. Then the deactivation is a result of the photoreactions (involving the production of free radicals or other photoproducts), and irreversible or reversible structural changes occur. Irreversible structural changes lead to molecular decomposition, which means that the UV absorbent is not characterized by good photostability [7]. A molecular mechanism of action of inorganic filters, like titanium dioxide and zinc oxide (TiO<sub>2</sub> and ZnO), is the UV radiation absorption, which in turn is overlaid with some scattering. Inorganic particles are characterized by a high energy gap between the valence and conduction bands (380-420 nm) [6].

An ideal sunscreen, in addition to strong radiation absorption, should dissipate excess energy by the appropriate routes. Molecules with more efficient mechanisms causing their return to their ground state without chemical changes are characterized by a lower risk of undesirable decomposition processes. The most desirable absorbents are compounds with a high rate of deactivation processes [6-8].

Photostability depends on degradation of UV filters. To put it simply, the reduction of UV radiation is carried out by the absorption of photons by the chromophore, i.e., the UV filter, which causes its excitation. An absorbing molecule dissipates energy in the form of heat or light, usually in a very short time. This may result also in the fluorescence or phosphorescence processes, which cause the return to the ground state. Isomerization, fragmentation, reactivity with other molecules, or the production of free radicals, reduce or eliminate the

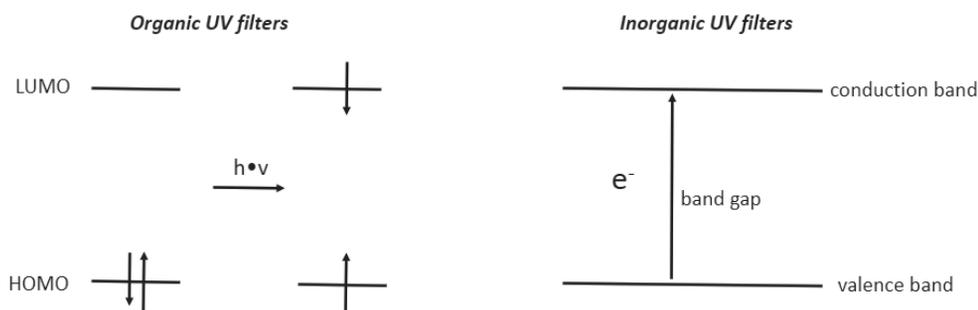


Fig. 1 Absorption mechanism in organic and inorganic filters Source: Own study

chromophore's ability to absorb energy, and, as a result, the UV filter is degraded.

In the photoprotective products based on organic filters, mixtures of several compounds are usually used, because no single compound provides an adequate protection against UVA and UVB radiation in their acceptable concentrations. It is very common to combine chemical and physical filters, although this requires prior research to avoid affecting the decomposition of organic filters with the production of toxic photoproducts [9].

### CLASSIFICATION OF SUNSCREENS ACCORDING TO THE TYPE AND PROTECTION LEVEL

The Polish Act on Cosmetic Products of 4 October 2018 (Ustawa o Produktach Kosmetycznych z dnia 4 października 2018 r.) [10] defines a UV-protective substance as a substance that protects the skin against the harmful effects of ultraviolet radiation. A sunscreen product is any preparation intended solely or primarily to protect from UV radiation by radiation absorbing, scattering, or reflecting [10, 11]. Such compounds are expected to be waterproof, photostable, as well as to have a small ability to penetrate deep into the skin, no further than to the stratum corneum. Additional requirements are not to induce allergic reactions, to be non-toxic, and safe for the skin [1].

Physical filters are compounds of mineral origin. They reflect radiation from the entire wavelength range. They form a protective layer on the surface of the skin against UV rays, so that they do not penetrate to the deeper layers of the skin [12]. These compounds exhibit a wider spectrum of protection, lower sensitizing properties, and greater photostability compared to organic filters [1, 13].

TiO<sub>2</sub> and ZnO protect against UVA and UVB radiation, but the scope of their protection is low in comparison to organic UV filters. The pigment particles are often coated with silicones, alumina, or fatty acids to reduce their accumulation, to facilitate their distribution on the surface of the skin [1], but above all to block their contact with water to inhibit the formation of free radicals.

Chemical filters are of single or multiple aromatic structures, sometimes coupled to carbon-carbon double bonds or

carbonyl groupings [14]. These compounds absorb some of the radiation, while reflecting the radiation with a wavelength higher than 380 nm, visible or infrared (IR). Organic filters are insoluble in water; therefore, they remain on the surface of the skin. They are also characterized by a large molecular weight which limits the penetration to the skin cells. Due to the above they do not pass through the stratum corneum [12].

Before any substance is approved for use as a sunscreen, it must undergo several tests confirming its action and safety. Only 2 inorganic and 74 organic compounds are approved for use in the European Union. Organic filters are benzophenones or derivatives of camphor, benzoylmethanes or paraaminobenzoic, salicylic, cinnamon, and anthranilic acids [11].

Of all the approved compounds, the 3 most controversial chemical filters, were selected for this study and their structures, properties, photostability and safety of use were analysed.

### AVOBENZONE

#### Physicochemical properties

Avobenzone (AVO) is the common name for 4-tert-butyl-4'-methoxydibenzoylmethane (Fig. 2). According to the INCI, (International Nomenclature Cosmetic Ingredient) – the nomenclature used for naming of ingredients of cosmetic products, the name of Avobenzone is Butyl Methoxydibenoylomethane. This compound is a whitish or yellowish crystalline powder with a faint odor. It dissolves well in oils, and does not dissolve in water [15]. The maximum absorption of UV radiation is shown for the wavelengths around 355 nm [16].

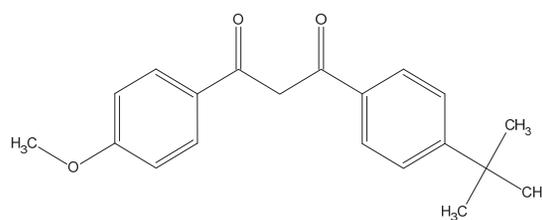


Fig. 2 Structure of Avobenzone Source: Own study

## Photostability

Avobenzone exists as two tautomers: enol and diketone. Due to the asymmetry of this compound, there are two forms of enols (Fig. 3).

Keto-enol isomerization is associated with a decrease in absorption in the UVA range (320-400 nm) and a simultaneous increase in absorption in the UVC range (260-280 nm). Upon the radiation, the enol form is photoisomerized into a diketone form. This process depends on the presence of oxygen.

The photostability of Avobenzone depends on the type of solvent [17]. It is photostable in polar protolytic solvents, whereas in polar aprotic solvents is unstable. The best solvent used in the photoprotection industry is mineral oil and/or isopropyl myristate [18]. In the absorption spectra of dissolved Avobenzone, two main bands are observed – the first one of maximum absorption at 350 nm and is attributed to the enol form, the second, much weaker band, with a maximum at 270 nm is considered to belong to the diketone form. With

increasing time of exposure to light, the intensity of the first band decreases, and the second band increases, which is associated with tautomerization, i.e., the mutual transition of the enol and diketone forms into each other under the influence of a certain factor (in this case light photons) or as a result of a spontaneous intramolecular reaction. The transformation of enol into diketone form may result from the transfer of a proton to an adjacent double bond. These isomers present the absorption bands as transition from bonding to anti-bonding molecular orbitals [19]. The  $\pi$ - $\pi^*$  transition bands move towards higher wavelengths as the solvent polarity increases. The maximum absorption of the enol form in polar solvents is located at higher wavelengths in relation to the maximum position in non-polar solvents. Due to the formation of the aggregates in water, a typical scattering profile is observed on the spectra for a colloidal suspension with a tail extending over longer wavelengths [20].

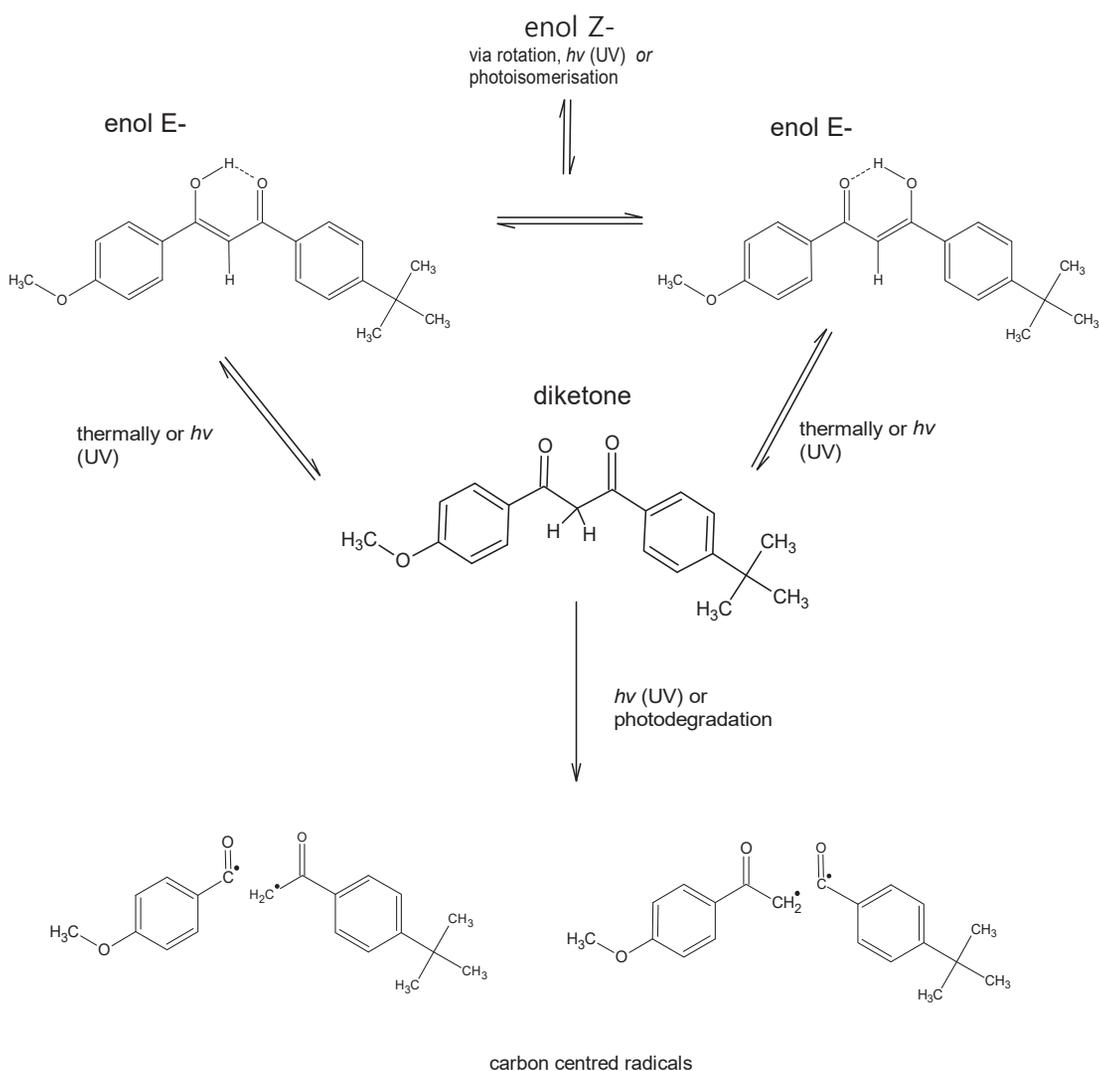


Fig. 3 Avobenzone in keto-enol equilibrium Source: Own study based on [17]

As aforementioned, the photodegradation leads to irreversible decomposition of Avobenzone and the formation of reactive oxygen species (ROS, e.g., singlet oxygen), therefore in the cosmetic products, this compound must be additionally stabilized. One of the methods of stabilization is the introduction of antioxidants. Their action is associated with the presence of free electrons, which can be given to unpaired electrons of free radicals. This extinguishes the reactive forms. The most popular compounds acting as stabilizers include vitamin C and vitamin E, as well as ubiquinone (coenzyme Q<sub>10</sub>). The stabilization effect depends on the concentration of antioxidants. A decrease in absorption in the UVA range is observed under the influence of radiation, i.e., a decrease in the effectiveness of photoprotection, however, it is lower than in the case of a pure compound. It must be pointed out that ubiquinone and vitamin E are promising options for increasing filter stability as well as SPF values without the need for additional substances [21].

Another stabilizing factor is the encapsulation of the molecule in the micelles. It is proved that the formation of micelles leads to disaggregation of Avobenzone. This form of stabilization does not fully prevent the diketone process, but depending on the surfactant chosen, it can reach a level of stabilization comparable to pure methanol. It is concluded that the insertion in micelles provides access to water molecules, which facilitate the restoration of enol form after photon absorption and relaxation [21].

To ensure maximum efficiency of the filter and thus directly control its photostability, various photo-stabilizers are combined (e.g. Octocrylene (INCI) with excited state quenchers (e.g. Ethylhexyl Methoxycrylene (INCI) [22].

### Safety

Studies on the safety of Avobenzone in sunscreen cosmetics have been ongoing since it was proven that the compound decomposes under the influence of UV radiation. There are reports of phototoxic potential, which may result from photoproducts formed by exposure to UV radiation [22]. Two main classes of photoproducts are specified: benzils (aromatic diketones) and arylglyoxals (aromatic derivatives of oxalic aldehyde), which are strong sensitizing agents [23]. In Avobenzone photodegradation process different classes of photoproducts of high sensitizing potential are created, which was confirmed by studies using photo-patch tests [24, 25]. The phototoxic potential was detected by one of the tests for the isolated compound, as well as in combination with other filters. Surprisingly, no similar results were observed during tests on a model of human skin. Acceptable photostability of cosmetic products containing this filter is, therefore, suggested [26].

Avobenzone is included in the list of substances approved for use in cosmetic products. Its maximum concentration in cosmetics is specified in Regulation 1223/2009 on cosmetic

products and is 5% [11]. SCCS (Scientific Committee on Customer Safety) confirmed the absence of estrogenic effects, potentially harmful to human health – this means that this substance does not affect the same receptors as the hormone and does not cause similar effects in the human body.

## OXYBENZONE

### Physicochemical properties and applications

Oxybenzone (BP-3, INCI: Benzophenone-3) (Fig. 4), or actually (2-Hydroxy-4-methoxyphenyl) (phenyl)methanone is poorly soluble in water but well in most organic solvents. It is found in the form of a white or yellow powder. It absorbs UV radiation in the UVA and UVB range [27].

This substance is used in many cosmetics, not only as a sunscreen. It can also be found in personal hygiene products (for example in shampoos and hair conditioners, anti-wrinkle creams, soaps, and bath oils), perfumes or color cosmetics (e.g., powders, mascaras) [28]. Its function is to absorb UV rays to prevent a decrease in the quality of cosmetic products.

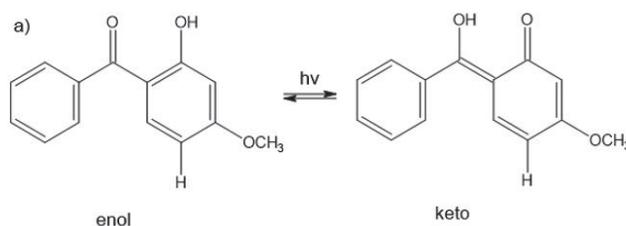


Fig. 4 Structure of Oxybenzone Source: Own study

### Photostability

BP-3 is characterized by high photostability, both in relation to UV and solar radiation, and significant absorption properties. On the absorption spectra of the compound there are 3 bands, with maxima at 241 nm, 288 nm, and 324 nm. The first two bands are the result of the presence of two benzene rings in the structure, while the third represents a keto-phenolic group in the molecule. Within 9 hours of exposure, the loss of absorption of this compound is less than 5%, and its photostability is not affected by the presence of a quencher, e.g. methionine. This filter has an effective mechanism of returning to the ground state after the transition into the excited state formed upon energy absorption by the enol form. After the energy is transferred to the molecule in the excited state, this state is quenched by internal conversion to the ketone form, and the energy is transferred again to the molecule in the ground state [19].

The pH of the environment strongly affects the stability of this sunscreen. Unlike anionic forms, neutral molecules prevailing in the aqueous solutions do not undergo photodegradation even after a long exposure time. During research on the deprotonated form of the filter, a significantly

reduced level of ray absorption in the range of 370-330 nm relative to the spectra of the neutral system was observed [29].

Based on studies of the influence of humic acid on the degradation of BP-3 under the influence of artificial sunlight, it was concluded that the degradation of BP-3 increases in the presence of this acid and is compared to direct photolysis in water. This phenomenon can be explained by the photosensitivity of the acid, which absorbs solar energy and generates radicals, which in turn can attack chemical compounds in water. The half-life of BP-3 in a pure aqueous solution is 433 days [30].

### Safety for human health and the environment

Consumer concerns about BP-3 in sunscreen products are about by the size of the molecule – it is small enough to penetrate the skin, and then enter the bloodstream. It was already shown that this compound can be carried by plasma carrier proteins, interact with human serum albumin, and displace drugs or other substances, which can cause disruptions in the proper functioning of the human organism. BP-3 is excreted from the body mainly in the urine, after binding to glucuronic acid [28]. The half-life of BP-3 in the organism is long, and it accumulates in the plasma [31].

There is an increasing number of reports of BP-3 toxicity, which were supported by studies on two living organisms – zebrafish (*Danio rerio*) and Chinese crucian carp (*Carassius auratus*). In both cases, changes related to the activity and structure of antioxidant enzymes were confirmed, as well as changes in glutathione concentration in *Carassius auratus* and increased concentration of free radicals in *Danio rerio* [32, 33]. An increase in lipid peroxidation processes and a decrease in antioxidant activity in the frontal cortex and hippocampus were also observed in female rats treated with BP-3 at a concentration of 100 mg/kg of body weight, which corresponds to the concentration in human plasma when using sunscreens containing the tested filter [34]. It shows that BP-3 can accumulate in the organism and generate oxidative stress.

BP-3 may also exhibit a negative impact on the functioning of tissues and organs, i.e. skin, kidneys, brain, endocrine and haematological systems, reproductive organs, as well as on the development of the fetus during pregnancy. The detectable levels were found in the urine and milk of nursing women and altered the morphology of the mammary gland was observed [28, 35]. According to the North American Contact Dermatitis Group, this filter is ranked among the three most common allergens in this group of cosmetic products [36]. All benzophenones are endocrine disrupting chemicals due to their affinity for steroid receptors, which can cause disturbances in the functioning of the gonads. In addition, these compounds are antagonists to androgen and progesterone receptors and may be inhibitors or stimulators in the production or metabolism of hormones [28].

According to the latest SCCS reports, BP-3 accumulates in large part in the liver of rats, where it can be converted to 2,4-dihydroxybenzophenone (BP-1) and possibly to (2-hydroxy-4-methoxyphenyl)(2-hydroxyphenyl)methanone (BP-8) as a result of enzymatic reactions, and BP-1 is a major metabolite also in humans [35]. The permissible concentration of BP-3 in sunscreen products is 2%, while in other cosmetics the maximum concentration is 0.5% [11]. In the NTP (*National Toxicology Program*, USA) studies, no changes in estrogen-responsive genes or adverse clinical signs were observed before or after childbirth [37]. *In vitro* and *in vivo* studies confirmed the absence of photomutagenic and photogenotoxic properties, as well as the fact that the compound is not phototoxic. It was observed that BP-3 does not stimulate the proliferation of breast cancer cells, but the long-term contact with a product of a sufficiently high concentration, increased migratory and invasive properties of two breast cancer cell lines. It is, therefore, suggested that it poses a risk of developing this type of cancer through endoplasmic transcriptional activation of genes conditioned by the reticulum. In addition, the compound does not affect the level of thyroid hormones and is not able to disturb their homeostasis. The substance is not corrosive or irritating to the skin or eyes.

The use of BP-3 has been prohibited in Hawaii, the U.S. Virgin Islands, and Palau since it poses a great threat to coral reefs. Corals exposed to BP-3 are bleached. This phenomenon is associated with a loss of membrane integrity and, as a consequence, a damage of pigments in zooxanthella [38], which remain in a symbiotic relationship with the coral. Moreover, it was also proved that this compound plays an important role in damage to coral larvae [39].

## OCTINOXATE

### Physicochemical properties

Octinoxate (OMC, INCI: ethylhexyl methoxycinnamate) is an ester of cinnamic acid (Fig. 5). It is a viscous, water-insoluble liquid, can be colorless or have a light yellowish color [40]. It absorbs UVB radiation in the wave range of 280-320 nm, although the low-energy tail of the absorption spectrum extends to the range corresponding to UVA, i.e., 320-400 nm [41].

### Photostability

OMC can be transformed from a *trans* into a *cis* isomer upon the radiation – which is the main pathway of the photochemical reactions of this compound (Fig. 6). The *Z*-form is characterized by a lower absorption capacity under the influence of UV radiation. The absorption spectrum of the *trans* isomer depends on the polarity of the solvent used, in contrary to the *cis* form, in which no similar relationship was observed.

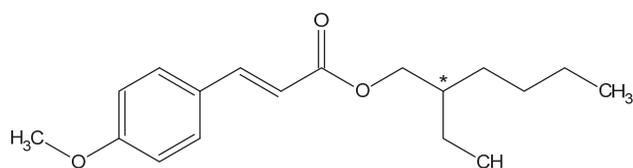


Fig. 5 Structure of Octinoxate (asterisk indicates the centre of chirality) Source: Own study

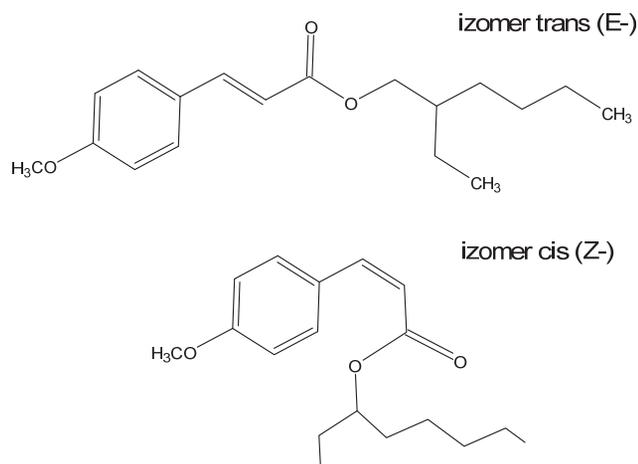


Fig. 6 Structure of the Octinoxate *trans* and *cis* isomers Source: Own study

In the absorption spectrum of diluted solutions of OMC, a band shift depending on the solvent is observed – the *trans* isomer shows maximum absorption at a wavelength of 291 nm in cyclohexane, while in methanol and ethanol the band maximum shifts to approx. 310 nm. Interestingly, the polarity of the solvent is relevant only in the case of the *E*-isomer, while in the *Z*- isomer the maximum is 305 nm, although the spectra between the solvents differ in half-width (the band is narrower in cyclohexane). Upon UVA and UVB, the range of absorbed radiation by the *trans* form in a non-polar solvent decreases dramatically, until the stationary state is reached. In this state, the absorption intensity is higher in a non-polar solvent than in a polar one. This suggests that in an organic solvent, photoisomerization is the predominant reaction, although additional photodegradation processes may occur.

Aggregation of OMC results in the formation of a long tail in the red range of the absorption spectrum, caused by a scattering of light by suspended particles. Aggregation of the *trans* molecules leads to an increase in polarizability. Upon radiation, 3 narrow bands with maxima at characteristic wavelengths appear on the spectrum, which indicates the formation of photoproducts, not only *cis* forms. Additional products, such as 4-methylbenzaldehyde and 2-ethylhexanol, are characterized by the absorption of higher energy values and, as consequence, reduced ability to absorb UVB radiation. This is due to the loss of conjugation - the phenomenon of overlapping one  $\pi$  orbital to another through the adjacent  $\sigma$  bond. As a result of photodegradation, transient products

may also be formed, the absorption of which is shifted towards the UVA region, which suggests the formation of compounds with greater conjugation. In summary, aggregation leads to rapid, irreversible degradation and the formation of a complex mixture of photoproducts.

The unfavourable reactions following the particles aggregation can be prevented by including antioxidants or excite state quenchers in the formula [41].

### Safety for human health and the environment

It was shown that OMC affects the endocrine system of humans and other organisms [42]. This compound has a similar endocrine effect as Oxybenzone. The negative effects are associated with a decrease in T4 levels, which is caused by the inhibition of 5'deiodinase, an enzyme that catalyzes the conversion of T4 to T3 [43]. Also, OMC can exhibit mild photoallergic properties [44] and is detectable in urine, serum, and breast milk [45]. However, according to SCCS, this compound is safe to use, because it is characterized by a low level of acute toxicity, and is not irritating or sensitizing, although in some cases it may be responsible for allergic dermatitis. The substance is not photomutagenic and its teratogenic dose is more than 500 mg/kg body weight per day [46].

Like Oxybenzone, OMC is not approved for use in some regions in the world, mainly in places with coral reefs. It contribute to their disappearance according to the mechanism that was presented earlier [37, 38].

### SUMMARY

Due to the growing awareness of the harmful effects of UV radiation, sunscreens have become a popular research object. The main aspects discussed include physicochemical properties, photostability, and safety of use.

All photoprotective compounds approved for use by the FDA (Food & Drug Administration) and the European Union meet all safety considerations but differ mainly in the level of photostability. SCCS provides more and more new, extensive opinions confirming all these aspects. To improve the level of photostability of cosmetic products, mixtures of mechanical filters, the additions of physical filters to organic compounds, or an increase in the number of UV filters are used. In the case of popular Avobenzone, an interesting approach is the use of photostabilizers and excited-state quenchers.

Some compounds may have a negative effect on the human endocrine system or show photosensitizing effects upon long-term use, due to their accumulation in the bloodstream. Their potential impact on other systems, internal organs, or fetal development during pregnancy is largely still a matter of speculation and requires more research. In addition, these compounds can have a detrimental effect on the aquatic environment and coral reefs. While in the case of Oxybenzone

and Octinoxate this is well documented, Avobenzone seems to be rather safe. Unfortunately, recent preliminary studies on this compound [47, 48] suggest that it may affect the environment and aquatic organisms in a fairly similar way.

## REFERENCES / LITERATURA

- Smyk P, Smyk E, Hołyńska-Iwan I, Olszewska-Słonina D. Połączenie filtrów naturalnych i sztucznych jako najlepsze źródło ochrony przeciwslonecznej w preparatach kosmetycznych. In: Górecki M, Górńska A, Ślachciak D. *Nauka niejedno ma imię*. Bydgoszcz: Wydaw. Ucz. UTP; 2016:220-221.
- Krzyżostan M. Ochrona przeciwsloneczna. Fakty i mity na temat działania filtrów slonecznych. *Cosmetic reporter*. 2018;7:12-26-128.
- Narayanan DL, Saladi RN, Fox JL. Ultraviolet radiation and skin cancer. *International Journal of Dermatology*. 2010;49:978-986. <https://doi.org/10.1111/j.1365-4632.2010.04474.x>
- UV Radiation. Centers for Disease Control and Prevention. <https://www.cdc.gov/nceh/features/uv-radiation-safety/index.html>. Accessed 18.03.2022.
- Radiation: Ultraviolet (UV) radiation. World Health Organization. [https://www.who.int/news-room/questions-and-answers/item/radiation-ultraviolet-\(uv\)](https://www.who.int/news-room/questions-and-answers/item/radiation-ultraviolet-(uv)). Accessed 18.03.2022.
- Osterwalder U, Herzog B. Chemistry and Properties of Organic and Inorganic UV Filters. In: Lim HW, Draelos ZD, eds. *Clinical Guide to Sunscreens and Photoprotection*. New York: Informa Healthcare; 2009:11-38.
- Rodrigues NDN, Staniforth M, Stavros VG. Photophysics of sunscreen molecules in the gas phase: a stepwise approach towards understanding and developing next-generation sunscreens. *Proceedings, Mathematical, Physical and Engineering Sciences*. 2016;472:1-29. <https://doi.org/10.1098/rspa.2016.0677>
- Rodzik-Czałka E. Nanostrukturalne fluorescencyjne materiały hybrydowe do konstrukcji biosensorów. Rozprawa doktorska. Kraków: Uniwersytet Jagielloński; 2018.
- Nałęcz-Jawecki G, Zawadzki T, Skrzypczak A. Substancje promieniochronne a środowisko przyrodnicze. *Biuletyn Wydziału Farmaceutycznego Warszawskiego Uniwersytetu Medycznego*. 2012;5:32-39.
- Ustawa z dnia 4 października 2018 r. o produktach kosmetycznych. Dz.U. 2018 poz. 2227. <https://isap.sejm.gov.pl/isap.nsf/DocDetails.xsp?id=W-DU2018000227>. Accessed 14.03.2022.
- Rozporządzenie Parlamentu Europejskiego i Rady (WE) nr 1223/2009 z dnia 30 listopada 2009 r. dotyczące produktów kosmetycznych (wersja przekształcona). <https://eur-lex.europa.eu/legal-content/PL/TXT/HTML/?uri=CELEX:32009R1223>. Accessed 14.03.2022.
- Stanisz B. Ochrona skóry przed negatywnymi skutkami promieniowania UV. *Farmacja Polska*. 2009;65(5):363-368.
- Serpone N, Dondi D, Albini A. Inorganic and organic UV filters: Their role and efficacy in sunscreens and sun care products. *Inorganica Chimica Acta*. 2007;360(3):794-802. <https://doi.org/10.1016/j.ica.2005.12.057>
- Chrisvert A, Salvador A. UV Filters in Sunscreens and other Cosmetics. Regulatory Aspects and Analytical Methods. In: Chrisvert A, Salvador A. *Analysis of Cosmetic Products*. Italy: Elsevier Science; 2007:83-120. <https://doi.org/10.1016/B978-0-444-52260-3.X5020-7>
- Avobenzone. PubChem. <https://pubchem.ncbi.nlm.nih.gov/compound/Avobenzone>. Accessed 12.03.2022.
- Bojarowicz H, Bartnikowska N. Kosmetyki ochrony przeciwslonecznej. Część I. Filtry UV oraz ich właściwości. *Problemy Higieny i Epidemiologii*. 2014;95(3):596-601.
- Murphy RB, Staton J, Rawal A, Darwish TA. The effect of deuteration on the keto-enol equilibrium and photostability of the sunscreen agent Avobenzone. *Photochemical & Photobiological Science*. 2020;19:1410-1422. <https://doi.org/10.1039/D0PP00265H>
- Vallejo JJ, Mesa M, Gallardo C. Evaluation of the Avobenzone photostability in solvents User in cosmetics formulation. *Vitae*. 2011;18(1):63-71.
- Abid AR, Marciniak B, Pędziński T, Sahid M. Photo-stability and photosensitizing characterization of selected sunscreens' ingredients. *Journal of Photochemistry and Photobiology A: Chemistry*. 2017; 332:241-250. <https://doi.org/10.1016/j.jphotochem.2016.08.036>
- Hanson KM, Cutuli M, Rivas T, et al. Effects of solvent and micellar encapsulation on the photostability of Avobenzone. *Photochemical & Photobiological Sciences*. 2020;19:390-398. <https://doi.org/10.1039/C9PP00483A>
- Afonso S, Horita K, Sousa e Silva JP, et al. Photodegradation of Avobenzone: Stabilization effect of antioxidants. *Journal of Photochemistry and Photobiology*. 2014;140:36-40. <https://doi.org/10.1016/j.jphotochem.2014.07.004>
- Nash JF, Tanner PR. Relevance of UV filter/sunscreen product photostability to human safety. *Photodermatology, Photoimmunology & Photomedicine*. 2014;30:88-95. <https://doi.org/10.1111/phpp.12113>
- Karlsson I, Hillerström L, Stenfeldt AL, et al. Photodegradation of dibenzoylmethanes: potential cause of photocontact allergy to sunscreens. *Chemical research in toxicology*. 2009;22(11):1881-1892. <https://doi.org/10.1021/tx900284e>
- Victor FC, Cohen DE, Soter NA. A 20-year analysis of previous and emerging allergens that elicit photoallergic contact dermatitis. *Journal of the American Academy of Dermatology*. 2010;62(4):605-610. <https://doi.org/10.1016/j.jaad.2009.06.084>
- Shaw T, Simpson B, Wilson B, et al. True photoallergy to sunscreens is rare despite popular belief. *Dermatitis*. 2010;21(4):185-198.
- Gaspar LR, Tharmann J, Maia Campos PM, Liebsch M. Skin phototoxicity of cosmetics formulations containing photounstable and photostable UV-filters and vitamin A palmitate. *Toxicology In Vitro*. 2013;27:418-425. <https://doi.org/10.1016/j.tiv.2012.08.006>
- Oxybenzone. PubChem. <https://pubchem.ncbi.nlm.nih.gov/compound/Oxybenzone>. Accessed 12.05.2022.
- Wnuk NG, Michalska K, Krupa A, Pawlak K. Benzophenone-3, a chemical UV-filter in cosmetics: is it really safe for children and pregnant women? *Advances in Dermatology and Allergology*. 2022;1(39):26-33. <https://doi.org/10.5114/ada.2022.113617>
- Wong NGK, Berenbeim JA, Hawkrigde M, et al. Mapping the intrinsic absorption properties and photodegradation pathways of the protonated and deprotonated forms of the sunscreen Oxybenzone. *Physical Chemistry Chemical Physics*. 2019;21(26):14311-14321. <https://doi.org/10.1039/C8CP06794E>
- Liu YS, Ying GG, Shareef A, Kookana RS. Photostability of the UV filter benzophenone-3 and its effect on the photodegradation of benzotriazole in water. *Environmental Chemistry*. 2011;8(6):581-588. <https://doi.org/10.1071/EN11068>
- Matta MK, Zusterzeel R, Nageswara RP, et al. Effect of sunscreen application under maximal use conditions on plasma concentration of sunscreen active ingredients. *JAMA*. 2019;321(21):2082-2091. <https://doi.org/10.1001/jama.2019.5586>
- Rodriguez-Fuentes G, Sandoval-Gio J, Arroyo-Silva A, et al. Evaluation of the estrogenic and oxidative stress effects of the UV filter 3-benzophenone in zebrafish (*Danio rerio*) Eleuthero-embryos. *Ecotoxicology and Environmental Safety*. 2015;115:14-18. <https://doi.org/10.1016/j.ecoenv.2015.01.033>
- Liu H, Sun P, Liu H, et al. Hepatic oxidative stress biomarker responses in freshwater fish *Carassius auratus* exposed to four benzophenone UV filters. *Ecotoxicology and Environmental Safety*. 2015;119:116-122. <https://doi.org/10.1016/j.ecoenv.2015.05.017>
- Skórkowska A, Maciejaska A, Pomierny B, et al. Effects of combined prenatal and adult benzophenone-3 dermal exposure on factors regulating neurodegenerative processes, blood hormone levels, and hematological parameters in female rats. *Neurotox Res*. 2020;37:683-701. <https://doi.org/10.1007/s12640-020-00163-7>
- Opinion on Benzophenone-3 (CAS No 131-57-7, EC No 205-031-5). Scientific Committee on Consumer Safety, European Commission. [https://ec.europa.eu/health/system/files/2021-04/sccs\\_o\\_247\\_0.pdf](https://ec.europa.eu/health/system/files/2021-04/sccs_o_247_0.pdf). Accessed 26.05.2022.
- Warshaw EM, Wang MZ, Maibach HI, et al. Patch test reactions associated with sunscreen products and the importance of testing to an expanded series: retrospective analysis of North American Contact Dermatitis Group data, 2001 to 2010. *Dermatitis*. 2013;24:176-182. <https://doi.org/10.1097/DER.0b013e3182983845>
- National Toxicology Program. [https://ntp.niehs.nih.gov/whatwestudy/testpgm/status/ts-10260-s.html?utm\\_source=direct&utm\\_medium=prod&utm\\_campaign=ntpgolinks&utm\\_term=ts-10260-s](https://ntp.niehs.nih.gov/whatwestudy/testpgm/status/ts-10260-s.html?utm_source=direct&utm_medium=prod&utm_campaign=ntpgolinks&utm_term=ts-10260-s). Accessed 15.05.2022.
- Danovaro R, Bongiorno L, Corinaldesi C, et al. Sunscreens cause coral bleaching by promoting viral infections. *Environmental Health Perspectives*. 2008;116(4):441-447. <https://doi.org/10.1289/ehp.10966>
- Danovaro R, Corinaldesi C. Sunscreen Products Increase Virus Production Through Prophage Induction in Marine Bacterioplankton. *Microbial ecology*. 2003;45(2):109-118. <https://doi.org/10.1007/s00248-002-1033-0>

40. Octinoxate. Pubchem. <https://pubchem.ncbi.nlm.nih.gov/compound/Octinoxate>. Accessed 18.05.2022.
41. Hanson KM, Narayanan S, Nichols VM, Bardeen CJ. Photochemical degradation of the UV filter octyl methoxycinnamate in solution and in aggregates. *Photochemical & Photobiological Sciences*. 2015;14:1607-1616. <https://doi.org/10.1039/c5pp00074b>
42. Ramos S, Homem V, Alves A, Santos L. Advances in analytical methods and occurrence of organic UV-filters in the environment – a review. *Science of the Total Environment*. 2015;526:278-311. <https://doi.org/10.1016/j.scitotenv.2015.04.055>
43. Klammer H, Schlecht C, Wuttke W, et al. Effect of a 5-day treatment with the UV-filter octyl-methoxycinnamate (OMC) on the function of the hypothalamo-pituitary-thyroid function in rats. *Toxicology*. 2007;238(2-3): 192-199. <https://doi.org/10.1016/j.tox.2007.06.008>
44. Darvay A, White IR, Rycroft RJ, et al. Photoallergic contact dermatitis is uncommon. *The British Journal of Dermatology*. 2001;145(4):597-601. <https://doi.org/10.1046/j.1365-2133.2001.04458.x>
45. Ruszkiewicz JA, Pinkas A, Ferrer B, et al. Neurotoxic effect of active ingredients in sunscreen products, a contemporary review. *Toxicology reports*. 2017;4:245-259. <https://doi.org/10.1016/j.toxrep.2017.05.006>
46. Opinion on the Evaluation of Potentially Estrogenic Effects of UV-filters adopted by the SCCNFP during the 17th Plenary meeting of 12 June 2001. European Commission. [https://ec.europa.eu/health/scientific\\_committees/consumer\\_safety/opinions/sccnfp\\_opinions\\_97\\_04/sccp\\_out145\\_en.htm](https://ec.europa.eu/health/scientific_committees/consumer_safety/opinions/sccnfp_opinions_97_04/sccp_out145_en.htm). Accessed 27.05.2022.
47. Boyd A, Stewart CB, Philibert DA, et al. A burning issue: The effect of organic ultraviolet filter exposure on the behaviour and physiology of *Daphnia magna*. *Science of The Total Environment*. 2021; 750:141707. <https://doi.org/10.1016/j.scitotenv.2020.141707>
48. Yujin Ka Y, Ji K. Waterborne exposure to avobenzone and octinoxate induces thyroid endocrine disruption in wild-type and thraa<sup>-/-</sup> zebrafish larvae. *Ecotoxicology*. 2022; 31: 948–955. <https://doi.org/10.1007/s10646-022-02555-1>

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