COSMETIC APPLICATION OF MICROFINE TITANIUM DIOXIDE

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Summary

The properties of titanium dioxide account for a broad use of this substance as a white pigment in numerous branches of industry, including cosmetic industry, as well as UV filter and semiconductor sensitizing photoreaction. Interaction of the TiO₂ particle and electromagnetic radiation are discussed. During the 1980-s and 1990-s numerous papers concerning semiconductor photocatalysis have appeared. They presented titanium dioxide as an active UVA and UVB absorber in result of which its surface became the source of free radicals – reactive oxygen species (ROS). The examples of these results are reported. Determination whether or not titanium dioxide can penetrate through stratum corneum during normal application of cosmetic products containing this compound is very important because of a risk of side-effects. Some papers of TiO₂ penetration in stratum corneum are reported.

Riassunto

Le proprietà del biossido di titanio giustificano l'uso diffuso di questa sostanza come pigmento bianco in numerosi settori dell'industria, incluso quello cosmetico, così anche come filtro UV e semiconduttore sensibilizzante delle fotoreazioni.

L'interazione tra le particelle di biossido di titanio e le radiazioni elettromagnetiche sono state in discussione.

Durante gli anni 80 e 90 sono apparse diverse pubblicazioni riguardanti semiconduttori fotocatalitici. Il biossido di titanio viene qui presentato come in grado di assorbire attivamente le radiazioni UVA e UVB, in questo modo la sua superficie diventa sorgente di radicali liberi - specie ossigeno.
reattive (ROS).
Esempi di questi risultati sono stati riportati nel lavoro in oggetto.
La determinazione del fatto che il biossido di titanio sia in grado o meno di penetrare attraverso lo strato corneo durante l'applicazione di prodotti cosmetici che lo contengono, è molto importante per via dell'eventuale rischio di effetti collaterali.
Sono stati riportati alcuni lavori che riguardano la penetrazione del biossido di titanio attraverso lo strato corneo.
INTRODUCTION

Titanium oxides, due to their variety of structure, properties and ultimate functionality, appear as fascinating non-organic solid compounds. Titanium Dioxide TiO₂ is very stable, insoluble in water and non-volatile, chemically and biologically passive. It appears in three different crystalline forms: rutile, anatase and brookite. The first two, rutile and anatase are the most interesting. Their crystalline structures could be described as chains of TiO₆ octahedra, in which each Ti⁴⁺ ion is surrounded by six O²⁻ ions. Both structures differ from each other by the level of similarity to a regular octahedron and an arrangement of octahedrons in chains. In rutile lattice structure each octahedron is in contact with ten neighbour ones sharing 2 edges and 8 corners, in the case of anatase - each octahedron is in contact with eight neighbour ones sharing 4 edges and 4 corners. As a result of those differences, distances between atoms, electron structure and physical properties of those substances differ as well. Both oxides have a very high reflectivity of light, they can absorb UV radiation and show surface activity in relation to numerous organic and non-organic compounds. They can be prepared in the form of particles of diameter between several and several hundred nm, colloidal systems and thin layer films. The properties mentioned above account for a broad use of titanium dioxide as a white pigment in numerous branches of industry, including pharmaceutical, cosmetic and food industry, as well as UV filter and semiconductor sensitizing photoreaction. Such variety of applications of one compound is possible because an interaction between that substance and electromagnetic radiation as well as results of that interaction depend on radiation wavelength, size and shape of particles and a characteristic of their surface.

INTERACTION OF PARTICLES AND ELECTROMAGNETIC RADIATION

Electromagnetic radiation, i.e. transport of energy in space includes waves between \(10^{-7}\) m and several thousand km in length. The most interesting for us, ultraviolet radiation is associated with wavelengths between 280 - 400 nm and a visible light's range between 400 - 760 nm. As indicated in Fig. 1, electromagnetic radiation can interact with the matter in various ways. It can alter a direction by deflection or scattering on a surface of the matter particles; it can be absorbed, transmitted and refracted while passing from one medium into another.

The scattering of radiation by homogenous particles has been described in Rayleigh's theory and Mie's theory. The conclusion of Rayleigh's theory is that for matter particles that are very small in comparison to the wavelength of the falling radiation (10-20 times smaller than the wavelength) the scattering intensity is inversely proportional to the power four of the wave-
The dependence concerning homogenous matter particles of any size can be derived from Mie's theory. Assuming that the thickness of the layer showed in Fig. 1 equals 1, and the concentration of spherical particles in a suspension equals \( c \), then the intensity of the radiation that falls on that layer and the transmitted one expresses the following dependence:

\[
\log \frac{I}{I_0} = qcl
\]

In this reasoning the intensity of specularly reflected radiation at the surface has been ignored considered as very low. Symbol \( q \) designates the extinction coefficient, which is the sum of scattering coefficient \( q_s \) and absorption coefficient \( q_a \).

\[
q = q_s + q_a
\]

The coefficients can be calculated on the basis of Mie's theory where the following values are taken into account: a wavelength of a falling radiation, a size of scattering particles, refractive indices of the substance and its environment. The extinction coefficient of particles consists of two parts: a real and an imaginary one. The latter one is responsible for absorption. Both parts of extinction coefficient change along with radiation wavelength.\(^{4,6}\)

A chemical compound molecule in a ground state has its valence electrons at HOMO orbital (highest occupied molecular orbital). After absorbing an energy quantum equal to the difference of energetic levels between HOMO and LUMO (lowest unoccupied molecular orbital) orbitals, an electron passes to LUMO orbital and the particle transforms into an excited state.

Fig. 2 illustrates a scheme model of energetic differences between HOMO and LUMO orbitals for semiconductors as number \( N \) of monomeric units in the particle increases from unity to more than 2000 units.\(^7\)

For many compounds, an increase of number \( N \) in a particle means a decrease of energy necessary to photoexcite the particle. For rutile and anatase particles the energy difference (\( h\nu = E_{bg} \)) between HOMO and LUMO orbitals amounts to 3.0 eV and 3.2 eV respectively, which is in accordance with UV range of wavelength. It means that titanium dioxide has an ability to absorb UV radiation and transform into the excited state. Free electrons \( e^− \) and holes \( h^+ \) appear then in a semiconductor particle.\(^8\)

**TITANIUM DIOXIDE AS A COSMETIC RAW MATERIAL**

**White pigment**

According to definition, pigments are solid molecules insoluble neither in water nor organic solvents; they reflect and scatter electromagne-
tic radiation within a range of UV spectrum and visible light spectrum. Titanium dioxide, the white pigment of exceptionally high refractive index (2.7 – 2.5), has been used in cosmetics industry as a component of colour cosmetics for decades. The average diameter of particles of those pigments amounts to 220 – 250 nm and more. They absorb and scatter UV and visible radiation in such a way that total effect of attenuation of radiation is similar within the whole range of the examined spectrum (Fig.3).4

UV radiation filter

Microfine titanium dioxide was introduced into the market at the beginning of the 1990-s. Microfine term refers to pigments whose particle diameters are between 20 – 100 nm. The pigment particles that are much smaller than visible radiation wavelengths, become practically transparent within visible range. On the other hand they attenuate UV radiation in a much more effective way. On the basis of Mie’s theory the extinction coefficient \( q \) can be calculated as a function of a wavelength and an average size of particles. The results of such approximate calculations for molecules of different diameters and for two chosen wavelengths are shown in Table I.

The data show that particles of microfine titanium dioxide attenuate UV radiation due to absorbance and scattering. For the wavelength at 310 nm it can be clearly noticed that the smaller particle’s diameter, the bigger participation of absorption coefficient. A very small particles, i.e. 20nm of diameter and less, should behave according to Rayleigh’s theory and scatter the shortest range of falling radiation in the most effective way.

<table>
<thead>
<tr>
<th>Average particle size</th>
<th>310 nm (UVB)</th>
<th>360 nm (UVA)</th>
</tr>
</thead>
<tbody>
<tr>
<td>nm</td>
<td>% qs % qa</td>
<td>% qs % qa</td>
</tr>
<tr>
<td>20</td>
<td>7 93</td>
<td>50 50</td>
</tr>
<tr>
<td>50</td>
<td>37 63</td>
<td>83 17</td>
</tr>
<tr>
<td>100</td>
<td>48 52</td>
<td>86 14</td>
</tr>
<tr>
<td>220</td>
<td>54 46</td>
<td>70 30</td>
</tr>
</tbody>
</table>

Pigmentary titanium dioxide is not suitable for UV protection though (from a point of view of cosmetics users) as it effectively interacts with a visible light. Formulations containing these particles are white and non-transparent.

Fig. 3 The spectra of microfine TiO₂ and pigmentary TiO₂ (schematic comparison).
TITANIUM DIOXIDE AS A SEMICONDUCTOR - SENSITIZER OF PHOTOREACTION

Destruction of chemical compounds and biological material

Absorption of electromagnetic radiation photon whose energy is equal or higher than \( hv = E_{bg} \) (Fig. 2) results in the promotion of an electron \( e \) from the valence band to the conduction band. At the same time in the valence band there is created the positively charged gap \( h^+ \). Recombination of \( e^+h^+ \) pair can take place on the particle surface or inside it. The energy surplus is emitted then in the form of heat and the excited molecule resumes its ground state. The other sequence of events is also viable: the electron and positively charged gap independently face the particle surface, where the electron reduces the electron acceptor molecule \( A \) to \( A^- \), a \( h^+ \) oxidizes the electron donor molecule \( D \) to \( D^+ \). (Fig. 4)\(^3\)

Fig. 4 Processes in the semiconductor particle.

Photocatalytic reactions occurring on titanium dioxide particles as the Fig. 4 indicates, has been broadly used in practice for removing organic and non-organic pollution from water and air and destruction of biological material.\(^8\)

Typical particle size of catalyst is 30 nm. The titanium dioxide activity can be modified by changing properties of its surface. The increase of catalysis effectiveness is usually achieved by deposition of other semiconductors, noble metals, colour organic compounds on titanium dioxide particles.\(^2\) In order to inhibit undesirable activity, the surface is covered with aluminium oxide, zirconium oxide, silicon oxide or other compounds.

EXAMPLES OF PROCESSES AND REACTIONS INDUCED BY UV RADIATION WITH A PRESENCE OF TITANIUM DIOXIDE USED IN COSMETICS

At the end of the 1970-s titanium dioxide started being considered as an effective and safe physical sunscreen as it was thought to be able to reflect and scatter rather than absorb visible and UV radiation.\(^9\) During the 1980-s and 1990-s numerous papers concerning semiconductor photocatalysis have appeared. They presented titanium dioxide as an active UVA and UVB absorber in result of which its surface became the source of free radicals - reactive oxygen species (ROS). Therefore interest has been raised concerning the safety of titanium dioxide applications in cosmetics.

Bio-molecules, cell and tissue cultures in vitro

There is no doubt that amino acids, purine and pyrimidine bases, DNA and RNA particles, enzymes placed in suspension containing titanium dioxide and exposed to UV radiation undergo degradation as most of organic compounds in such conditions do.\(^10\) In studies concerning genetic material damages, water solutions of citosine, thymine, uracil as well as ade-
nine, guanine and titanium dioxide P25 (80% anatase, 20% rutile; average particle size 20 – 40 nm) saturated with oxygen have been exposed to a mercuric lamp’s radiation (over 290 nm UVA + UVB). Similarly DNA and RNA particles have been irradiated with radiation 310 – 400 nm in water suspension with and without titanium dioxide. Researchers observed that decomposition of examined nucleic acids has been occurring 500 – 800 times more efficiently with titanium dioxide. The authors of a paper concerning inactivation of horse radish peroxidase wrote: “clearly the presence of TiO₂ does not protect the enzymes from damage, but rather, it helps inactivation to occur much more efficiently”. Examination of the influence of irradiated titanium dioxide on animal cell and tissue cultures leads to less univocal conclusions. The influence of various types of titanium dioxide (anatase 21 nm, anatase 255 nm, rutile 255 nm, rutile 42 nm) on cell cultures has been examined in vivo. Samples have been exposed to radiation similar to the natural sunlight. It has been observed that titanium dioxide sensitised by radiation has damaged DNA and caused chromosome structural aberrations in mammalian cell cultures. Genotoxic activity was dependent on radiation intensity, concentration and type of dioxide – the most active was anatase 21 nm, the least rutile 41 nm; anatase 255 nm was active also without radiation. In the other paper the authors have not observed a negative influence of titanium dioxide on genetic material of normal and cancer human cells, but the conditions of the examination were different (TiO₂ microfine anatase: UVA 360 nm). The authors showed that the same dioxide protects cells against the effects of UVC 254 nm radiation. The differences in titanium dioxide activity are associated with a crystalline form and particle size. It has been observed that anatase exposed to radiation of wavelength 370 nm usually generated more hydroxyl radicals than rutile and amorphous form; for anatase the most active was the form in which crystal size was around 30 nm, for rutile around 90 nm. It should be stressed that all quoted studies have used titanium dioxide with uncovered surface.

METHODS OF COMPARISON OF ACTIVITY OF DIFFERENT OXIDES

Titanium dioxide particles can be covered with zirconium oxide, aluminium oxide, silicon oxide and many organic compounds. Those additives influence surface properties of titanium dioxide and change its photocatalytic activity. There are not many studies that compare photocatalytic activity of modified surface dioxides in a systematic way. Comparison of different materials’ activity is usually based on examination of oxygenation reactions of model systems or indication of free radicals concentration generated by radiation influence. The example of the first approach to this issue can be oxygenation of acetaldehyde to acetic acid with a presence of several types of photocatalysts and UV radiation of wavelength 360 nm. The compounds used in the studies are listed in Table II:
## Table II

**Sample of titanium dioxide**

<table>
<thead>
<tr>
<th>Sample</th>
<th>Crystalline form</th>
<th>Average size</th>
<th>Type of raw material</th>
<th>Non-organic covering</th>
<th>Organic covering</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Anastase 70% rutile 30%</td>
<td>21 nm</td>
<td>Microfine</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>B</td>
<td>Anastase</td>
<td>410 nm</td>
<td>Pigment</td>
<td>None</td>
<td>Polyethylene or methicone or dimethicone or STPM*</td>
</tr>
<tr>
<td>C</td>
<td>Rutile</td>
<td>30-50 nm</td>
<td>Microfine</td>
<td>Al₂O₃</td>
<td>Lecithin or dimethicone</td>
</tr>
<tr>
<td>D</td>
<td>Rutile</td>
<td>180-800 nm</td>
<td>Pigment</td>
<td>None</td>
<td>Poliol</td>
</tr>
</tbody>
</table>

*combination of esters of glycerine, octyldodecyl myristate and dimethicone

It appeared that in this reaction the most active catalyst was pigment B with non-covered surface, then oxide A. Covering pigment B with polyethylene decreased the activity by four times and with dimethicone or combination of organic compounds the activity almost disappeared. Similar behaviour has been observed with oxide C – in this case there was no non-covered sample and fairly low activity of the sample covered with Al₂O₃ has been compared with several times lower activity of the same type of oxide covered with lecithin and dimethicone. Other results have been obtained in tests of oxygenation of corn oil and squalen in water-ethanol suspension. The samples have been irradiated with a lamp imitating the sunlight. It has appeared that under an experimental condition the double bonds were protected against oxygenation by titanium dioxide covered by aluminium oxide and silicon dioxide or aluminium oxide and glycerine. The samples covered with aluminium hydroxide and stearic acid, dimethicone, aluminium oxide and stearic acid appeared to be oxygenation promotors, sometimes more effective ones than dioxide sample with non-modified surface.

Photoactivity of titanium dioxide samples can be compared by indication of, for instance, concentration of singlet oxygen or hydroxyl radical by a method of spectroscopy. It has been observed that in the first case titanium dioxide covered with methylhydrogen polysiloxane and irradiated with a xenon lamp was not photoactive in ethanol suspension. However the authors at the end of their article wrote sentence that sounded like a warning: “Because TiO₂ has been used as a potent sunscreening agent, biologic significance of the photodynamic properties of this compound to generate singlet oxygen and super oxide anion should be taken into account for preventing oxidative damage of the skin.”

### PENETRATION OF TITANIUM DIOXIDE MOLECULES THROUGH STRATUM CORNEUM

Determination whether or not titanium dioxide can penetrate through stratum corneum during normal application of cosmetic products contai-
ning this compound is very important because of a risk of side-effects.\(^{19}\) The studies examining this subject have been published since the mid-1990s. Penetration of microfine titanium dioxide (average molecule size 20 – 60 nm) suspended in water, polyethylene glycol and castor oil through a rabbit skin has been examined and some titanium dioxide ability to pass percutaneously particularly from oily suspension has been observed.\(^{20}\) Several papers concerning penetration of dioxide through human epidermis in vivo and in vitro have been published.\(^{21,22,23}\) Titanium dioxide penetration has been studied by a method of tape stripping. Atomic absorption spectrometry (AAS) and transmission electron microscopy (TEM) have been used to analyse the obtained samples. The presence of micropigment molecules has been observed in the succeeding 10 – 12 layers of stratum corneum. It has been also observed that the form of examined compound had a significant influence on penetration effect: the compound from oily suspension penetrated deeper than from a water suspension; the greatest effect could be obtained by liposomes application.\(^{22,23}\) Possible photocatalytic activity of titanium dioxide particles within stratum corneum raises understandable suspicions that only partially can be dispelled by the results of the studies on durability of covering TiO\(_2\) with aluminium oxide. (Aluminium oxide appeared to be permanently bound to the surface of examined TiO\(_2\) samples and a ratio between aluminium and titanium has not been changing either in formulation preparing process or in particles that penetrated into stratum corneum of epidermis.)\(^{24}\)

**CONCLUSION**

Titanium dioxide, depending on particle size, can scatter and reflect visible light and/or UV radiation. The particles of TiO\(_2\) smaller than 100 nm are practically transparent for a visible light, and because of their ability to scatter radiation of shorter wave-length they have been broadly applied as UV filters. However the initial convictions that titanium dioxide is chemically and biologically passive and that it does not penetrate through the epidermis in topical applications are not entirely compliant with some experimental data published during the last decade.

Titanium dioxide absorbs UV radiation and heat emission is not always the only effect of this absorption; frequently as an active semiconductor it initiates occurring free radicals (ROS - reactive oxygen species predominantly), that can be harmful for both components of cosmetics and the skin the preparation is applied on. Publications concerning photoactivity of titanium dioxide particles with modified surface sometimes show contradictory data regarding effectiveness of different covering substances. The reason of this can be that the experimental conditions of particular studies cannot be compared to each other straightforwardly or the authors did not include all possible factors influencing the activity of titanium dioxide as a photocatalyst in their conclusions. The number of reports concerning penetration of small titanium dioxide particles into stratum corneum of epidermis is also increasing.

The problems that microfine titanium dioxide creates for chemists, technologists and physiologist are sure to be broadly studied in the future.
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