

## CHAPTER I

### INTRODUCTION

Sunlight consists of a wide spectrum of radiation, from which only a narrow bandwidth between approximately 400 to 800 nm remains visible to the human eye. The longer wavelengths beyond 800 nm are felt by human as heat radiation or infrared. In the range shorter than visible wavelength we find the ultraviolet (UV) spectrum. The UV radiation can be further divided into four major bands; vacuum UV, UVC, UVB and UVA<sup>1</sup> (Fig. 1.1). The vacuum UV is radiation with a wavelength less than 200 nm. The UVC occupied the region between 200 and 280 nm. Neither vacuum UV nor UVC reach the surface of the earth because of the absorption by ozone layer. On the other hand, the UVB (280-320 nm) and UVA (320-400 nm) can penetrate the ozone layer. The UVB radiation promotes vitamin D synthesis and increases skin pigmentation or tanning.<sup>2</sup> At the same time, UVB triggers various serious skin damages depending on light intensity and skin sensitivity. UVB inhibits or interferes DNA, RNA and protein synthesis, induces early and prolonged erythema responses that would lead to photoaging and skin cancer.<sup>3</sup> The effects from UVB require no intermediate photosensitizer because nucleic acids, proteins and many biological molecules can directly absorb UVB radiation.<sup>4</sup> As UVB is known for not passing through glass. A sturdy piece of window glass can help prevent most of these undesired responses.

The UVA which occupies the region between 320 and 400 nm can produce a significant amount of photoinduced biological effects. The UVA indirectly damages cells through the reactive oxygen species.<sup>4-6</sup> UVA ray also influences a direct pigmentation and increases the biological effect from the UVB.<sup>2</sup> They induce both an immediate erythema, which diminishes within 2 hours and a delayed erythema response which reach a peak at 6 hours. This is opposite to the UVB induced delayed erythema which tends to reach a peak in 12 to 24 hours.<sup>3</sup> Although UVA is less energetic than UVB, it can, however, penetrate deeper into the dermis (Figure. 1.2), while UVB can penetrate only into the stratum corneum and the epidermis. Both UVA and UVB contribute together to make photoaging and skin cancers.

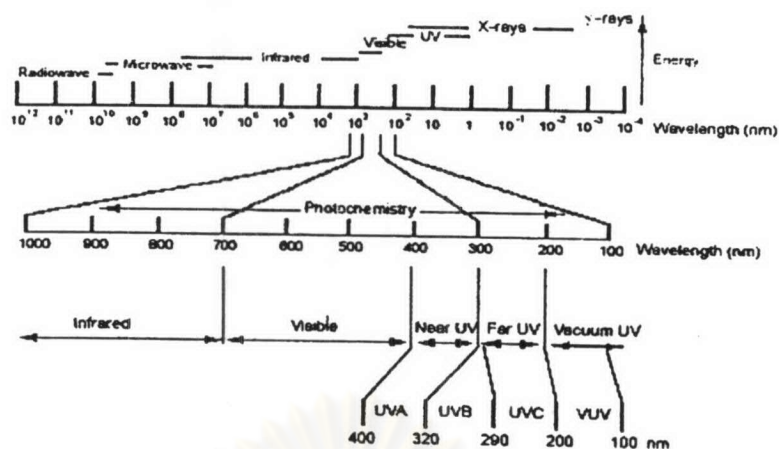


Figure 1.1 Electromagnetic spectrum

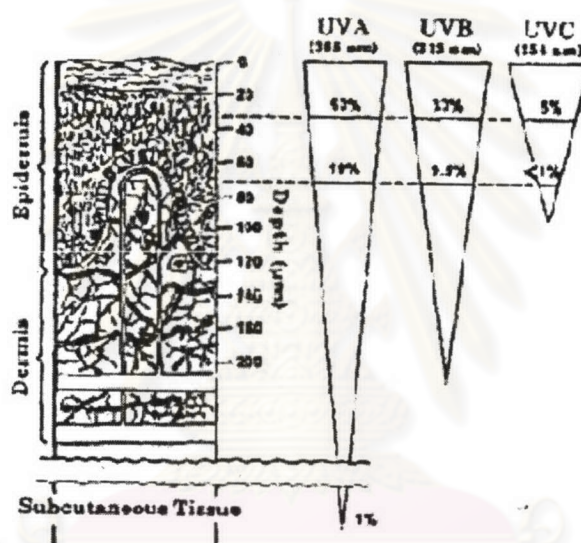


Figure 1.2 UV penetration into the skin

Although the simplest strategy for protection from the harmful effects of UV is avoidance. The most convenient, sufficient and practical strategy for UV protection is the use of sunscreen chemicals.

## 1.1 Sunscreen Chemicals Characters<sup>2</sup>

### 1.1.1 Absorption Range

Good sunscreen chemicals have to absorb the radiation in the range which harmful for human. Practically a choice is made between one or more UVB sunscreens. As a result, a certain bandwidth filter usually corresponds to a combination of UVB and UVA sunscreens.

### 1.1.2 Solubility

Whether a sunscreen is based on oil or aqueous gel, the chosen sunscreen compound must be compatible with its base. In the case of emulsion, sunscreen either water or oil soluble compounds can be used. Often a combination of water and oil soluble sunscreen is desirable due to cost or effectiveness considerations.

### 1.1.3 Sun Protection Factor (SPF)

SPF is a ratio of the amount of UV radiation that produce erythema in skin covered by sunscreen to the amount of UVB radiation that produce a similar erythema in skin uncovered by sunscreen. The SPF value corresponds to the ability of sunscreen to protect against UV radiation.

## 1.2 Classification of Sunscreen Chemicals<sup>3</sup>

Sunscreen chemicals may be classified according to the type of protections, either as physical blockers or chemical absorbers.

### 1.2.1 Physical Blockers

A physical blocker is a chemical that reflects or scatters the UV radiation. Examples of physical blockers include zinc oxide, titanium dioxide, and red petrolatum. Physical blockers, if present in sufficient quantities, will reflect all the UV radiation. They are currently being used in conjunction with chemical absorbers to achieve high sun protection factors (SPF).

There are, however, still many debates on the safety of physical blockers. Titanium dioxide ( $\text{TiO}_2$ ) has been reported to produce hydroxy radical under UVA irradiation and, therefore, can induce cytotoxicity.<sup>7-8</sup> Since  $\text{TiO}_2$  exhibits semiconductor properties, they have been used as photocatalyst for the degradation of organic pollutants in waste waters. Some investigators have shown that photoexcited titanium dioxide can cause cell death both *in vitro* and *in vivo*.<sup>9</sup>

### 1.2.2 Chemical Absorbers<sup>2-3</sup>

Chemical absorbers are organic molecules whose absorption bands are in UV region and help absorb the harmful UV radiation.

*UVA absorbers* are chemicals that absorb radiation in the 320-360 nm region of the UV spectrum. Examples of UVA absorbers include benzophenone, anthranilate, and dibenzoyl methane.

*UVB absorbers* are chemicals that absorb radiation in the 280-320 nm region of the UV spectrum. Examples of UVB absorbers include *p*-aminobenzoate (PABA) derivatives, salicylate, cinnamate and camphor derivatives.

The chemical absorbers used in sunscreen industry, can be classified into 7 categories (Figure. 1.3):

- A. cinnamate derivatives
- B. *p*-aminobenzoate derivatives
- C. salicylate
- D. benzophenone
- E. camphor derivatives
- F. dibenzoylmethane
- G. anthranilate

ศูนย์วิทยทรัพยากร  
จุฬาลงกรณ์มหาวิทยาลัย

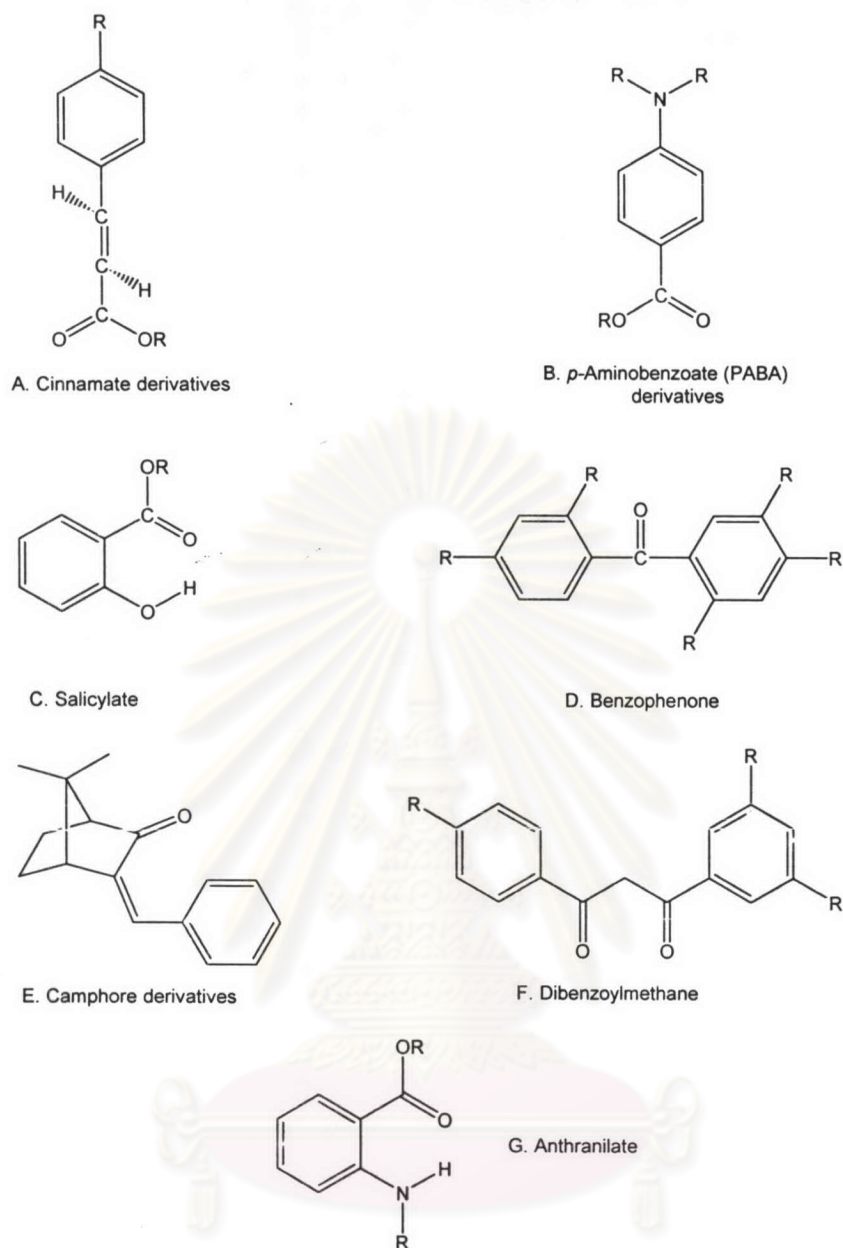


Figure 1.3 The sunscreen absorbers used in the sunscreen industry

### 1.3 Mechanism of Sunscreen Action<sup>3</sup>

Sunscreen chemicals are generally aromatic compounds conjugated with a carbonyl group. In many examples, an electron releasing group such as amine or methoxy group is substituted in the ortho or para position of the aromatic ring. They absorb the harmful short-wave (high energy) UV rays (280-390 nm) and convert the remaining energy into longer wave (lower energy) radiation (usually above 700 nm). The process of sunscreen action is called “photophysical process”, not a photochemical process and ideally no change in molecular structure should be

observed. Mechanism of sunscreen action (Figure 1.4.) involves excitation of electron from ground state by absorbing the UV rays. Then upon the return of electron from excited state to ground state, the absorbed energy is emitted in the form of IR or heat.

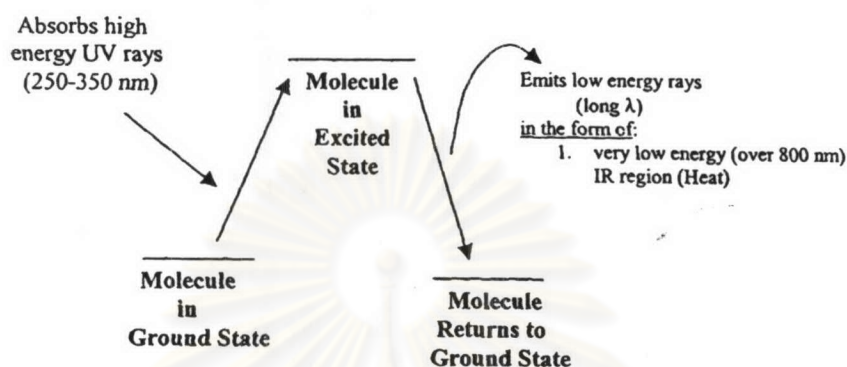


Figure 1.4 Mechanism of sunscreen action

## 1.4 Factors affecting the UV Absorbance of Sunscreens

### 1.4.1 Effect of pH

The UV absorption spectra of acidic and basic compounds are affected by pH. In the case of acidic compounds, the use of alkaline conditions (pH over 9) will result in the formation of anions that tend to increase delocalization of electrons. This electron delocalization decreases the energy required for the electronic transition in the UV spectrum, and hence a bathochromic shift is observed (longer wavelength). On the other hand, acidic conditions (pH below 4) will result in the formation of cations with aromatic amines. A hypsochromic shift (toward lower wavelength) occurs since the protonation of the unbounded lone pair electrons decreases resonance delocalization of the electrons.

### 1.4.2 Effect of Solvent

The use of different solvents in cosmetic formulations may profoundly influence the effectiveness of a sunscreen chemical. If the sunscreen is polar, then interactions with polar solvents will be quite extensive. This interaction with solvent stabilizes the ground state, thereby inhibiting electron delocalization. The net result would be a hypsochromic shift to lower wavelength. In contrast, if the sunscreen is less polar, then interactions with

polar solvents would be stronger at the excited state, which is more polar than the ground state. This then lowers the energy requirements for the electronic transition; hence, a higher maximum wavelength ( $\lambda_{\text{max}}$ ) would be expected, and bathochromic shift occurs.

### 1.5 Effect on the Extinction Coefficient

The effectiveness of a sunscreen chemical is assessed through the value of the extinction coefficient. Chemicals with high extinction coefficient values are more efficient in absorbing the energy of the harmful UV radiation than those with lower extinction coefficient values. Electronic transitions for any compounds may be characterized as symmetry allowed or forbidden. Symmetry allowed transitions generally have high extinction coefficients while symmetry forbidden transitions have lower extinction coefficients. The degree of resonance delocalization in a molecule can be used to predict the relative  $\lambda_{\text{max}}$ . A similar qualitative prediction for extinction coefficient is also possible. Usually the extinction coefficient values are reported in terms of "Molar Extinction Coefficient" or sometimes called "Molar Absorption Coefficient" or  $\epsilon$ . The  $\epsilon$  value is obtained experimentally using Beer's law:

$$A = \epsilon bc$$

where A is absorbance

b is the cell path length (1 cm)

c is the concentration of the absorbing species in mol per litre

### 1.6 Silicones<sup>10</sup>

Silicones have been part of the cosmetic and toiletries industry since 1940s. The first use of polydimethylsiloxane or dimethicone (Figure 1.5) was in a protective skin care which known as silicare by Revlon<sup>11</sup>. Incorporation of silicones into hair care products followed shortly thereafter, dating back to early 1950s. The low surface tension and lubricious nature characteristic of silicone fluid rendered these materials excellent additives in personal care products that helps reduce drag and impart a velvety soft feel to hair and skin. Figure 1.5 shows the chemically structure of polydimethylsiloxane (PDMS), or dimethicone, the first commercially available silicone product. The length of the polymer may vary to give dimethicones of different molecular weights and viscosities,

providing a range of properties.<sup>12</sup> Normally, all these silicones are clear, colorless and insoluble in water.

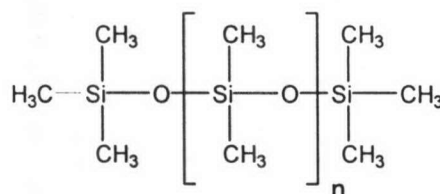


Fig 1.5 Polydimethylsiloxane (PDMS) or dimethicone

In general, the substantive properties of silicones relate to fundamental properties of their polymeric structures. The most important properties with regard to cosmetics and toiletries are shown below.

#### 1.6.1 A High Spreading Coefficient<sup>i</sup>

High spreading coefficient, along with a low interfacial tension against lipids, allow intimate contact with and wetting of proteinaceous surfaces. The ability of a silicone to form a thin, cohesive film is a necessary factor for the development of substantivity.<sup>ii</sup>

#### 1.6.2 Solubility

The solubility of dimethicones make these fluids insoluble in many aqueous and organic systems such as in ethanol, a property that often frustrates cosmetic chemists. However, with the development of functionalized silicones, this problem can be solved. For example, grafting of polar functional groups on silicones can make them soluble in more polar organic systems.<sup>10</sup>

#### 1.6.3 Variable Rheological Properties

The well known ability of PDMS to polymerize to various degrees provides polymers at a wide range of molecular weights and solubility. Usually, physical resistance<sup>iii</sup> increases with viscosity.

The unique properties and benefit afforded by silicones in personal care products became increasingly evident. But their usage remained quite limited due to their inherent solubility and incompatibility problems. With the advent of

<sup>i</sup> Spreading Coefficient refers to the ability of substance to spread over certain surface. Ideally, monolayer film is preferred.

<sup>ii</sup> Substantivity refers to permanence and endurance of substance on certain surface.

<sup>iii</sup> Physical resistance refers to the resistance properties of substance as thermal and electricity resistance.



new polymeric thickeners and suspending agents, silicone emulsifiers, and organomodification of the silicone polymer themselves, the uses of silicones in personal care products have dramatically increased in recent years. It has been estimated that half of all new personal care products introduced into the marketplace in 1994 contained at least one type of silicone in formulation.<sup>11</sup> Today, there is a wide variety of silicone products available that provide numerous benefits in personal care formulations.

In both skin care and hair products, silicones are recognized for their lubricating properties and the characteristic soft, smooth feel that they impart. These versatile fluids can provide substantivity and durability as well. Moreover, in skin care applications, silicone resin additives increased resistance to be washed off. In hair care products, organofunctional silicones, particularly those with amine functionality, provide substantive, durable conditioning properties.

## 1.7. Literature Reviews

### 1.7.1 Sunscreen

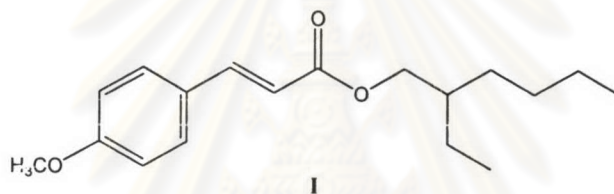
Sunscreens are widely used to reduce sunburn, photoaging, and skin cancer. Sunscreen products are routinely tested for their ability to delay the onset of erythema (sunburn) in skin exposed to UV radiation. Regulatory requirements for the approval of sunscreens are varied. In the USA, sunscreens are regarded as drugs whereas in Europe they are classified as cosmetics. The majority of the commercially available sunscreens today are a combination of agents from several chemical groups. Para-amino benzoic acid (PABA) was an early chemical sunscreen agent that was frequently associated with contact<sup>iv</sup> and photo contact<sup>v</sup> sensitivity reactions, had poor substantivity characteristics, often discolored clothing and was toxic. This compound is rarely found in sunscreen formulation today. Other sunscreen agents include compounds from the salicylate, cinnamate, benzophenone, anthranilate, and dibenzoylmethane groups. Among them, cinnamate derivatives are the most widely used sunscreen compounds in many countries. Many research groups have demonstrated that octyl methoxycinnamate (OMC) is quite safe concerning allergic contact (AC) and photoallergic (PA) effects of the compound.<sup>13-14</sup> This makes OMC now the most widely used UVB filter in cosmetic formulation worldwide.

---

<sup>iv</sup> Contact sensitivity reaction refers to the sensitive condition on skin when contacts with a substance without light stimulation.

<sup>v</sup> Photo contact sensitivity reaction refers to the sensitive condition on skin when contact with a substance with light stimulation.

In 2001 A. Darvay and coworkers<sup>13</sup> analyzed data from 2715 patients who underwent photopatch testing at St. John's Institute of Dermatology during the period of 1983-1998. The results show a low yield of positive photopatch test.<sup>vi</sup> Thus, despite the large increase in the use of OMC over the last decade, the development of photoallergen (PA) reactions remains rare. Furthermore, most of the common UV filter photoallergens identified in this study, including PABA, amyl dimethyl PABA and benzophenone-10, are now rarely used in sunscreen manufacture, while isopropyl dibenzoylmethane was voluntarily removed from the market in 1993. Currently, benzophenone is the most common contact photoallergen still in use. In contrast, during 1996-1997 C. Ricci and coworkers<sup>14</sup> did the patch<sup>vii</sup> and photopatch tests on 36 patients which were 12 males and 24 females, age range 22-83 years with relapsing contact dermatitis of the face, arms, hands, and other sun-exposed areas. Only 1 positive test result to OMC was observed.



Nevertheless, many reports have shown that substantial amounts of applied cinnamate derivatives, can be absorbed into human's skin layers.<sup>15-18</sup> For examples, in 1995 U. H. Leweke and B. C. Lippold<sup>15</sup> found the absorption of isoamyl-4-methoxycinnamate into the human skin. Similarly in 1997 C. G. J. Hayden and coworkers<sup>16</sup> reported that OMC was absorbed through the skin layers. In this study, OMC could be recovered from milk of human volunteers.

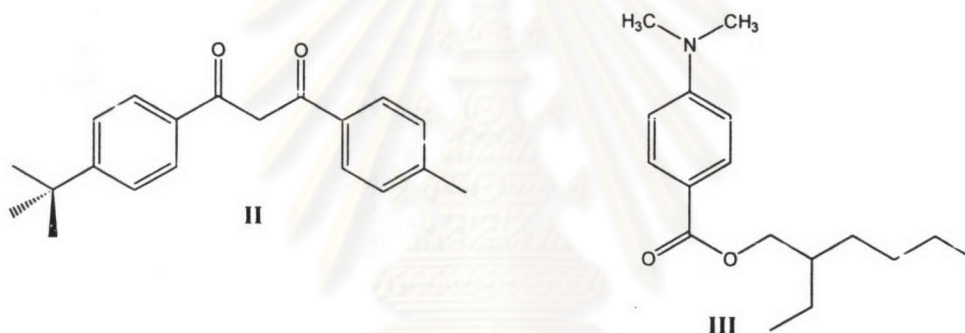
F. Benech-Kieffer and coworkers<sup>18</sup> studied the percutaneous absorption of OMC sunscreens *in vitro*. OMC absorptions were detected in both pig and human. The correlation of the quantitative data between pig skin and human skin was very good. This research confirmed the OMC absorption through both pig's and human's skin layers.

Since many studies have shown that OMC can be absorbed into the body. Toxicity of OMC is now started to be a concern.<sup>19-20</sup> In 1999 X. Chunxia and coworkers<sup>19</sup> reported that OMC, octyl *p*-dimethylaminobenzoate and oxybenzone (OB) could inhibit cell growth and DNA synthesis.

<sup>vi</sup> Photopatch test refers to a test for allergic reaction of a substance on skin when exposed to a light source.

<sup>vii</sup> Patch test refers to a test for allergic reaction of a substance on skin without being exposed to a light source.

Beside the absorption problem, photostability of UV filters should also be addressed here.<sup>21-25</sup> For example, in 1990 N. A. Shaath and coworkers<sup>21</sup> studied the stability of various UV filters under UV light. It was shown that butylmethoxy dibenzoylmethane (**II**) and octyl dimethyl PABA (**III**) significantly degraded in ethanol/water mixture. Octyl dimethyl PABA which dissolved in isopropylmyristate (IPM) exhibited 52.8 percentage of photochemical degradation. Also, OMC showed moderate degradation in mineral oil, IPM and ethanol/water mixture. Similarly, in 1999 N. Tarras-Wahlberg and coworkers reported that octyl dimethyl PABA, butylmethoxy dibenzoylmethane and OMC were not stable against UV irradiation.<sup>22</sup> Their UV absorbance decreased rapidly upon additional exposure to UV light. In 2001, S. Pattanaargson and P. Limpong<sup>23</sup> demonstrated that a *trans*- (*E*) to *cis*- (*Z*) configurational change of OMC does occur upon light exposure and its photoisomerized product, *cis*-OMC, was isolated (Figure 1.6).



Moreover, kinetics study of *cis/trans* photoisomerization of OMC indicates that the photostationary equilibrium will shift to more *trans* configuration in more hydrophobic medium.<sup>26</sup>

ศูนย์วิจัยทรัพยากร  
จุฬาลงกรณ์มหาวิทยาลัย

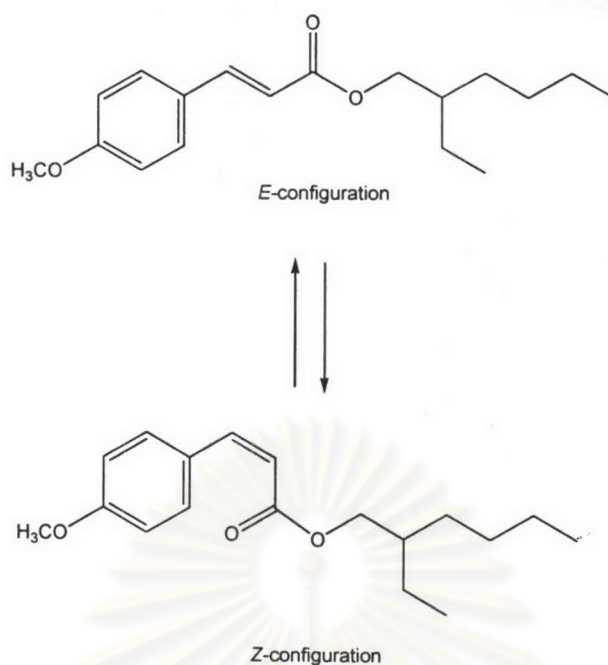


Figure. 1.6 conversion of (*E*)-OMC to (*Z*)-OMC after exposure to UV radiation

### 1.7.2 Silicone

Several decades ago, chemists in formulation industry wishing to work with silicone materials were limited to dimethicone polymers or cyclomethicone fluids. The very low absorption through skin, very low toxicity, low surface tension and lubricious characteristic of silicones render these materials excellent additives in personal care products since 1940s. They help reduce drag and impart a velvety soft feel to hair and skin. Today a wide variety of silicone products is available for the formulations that provide numerous benefits in personal care industry. These special silicones are called “functionalized silicones”,<sup>10</sup> which are polysiloxane grafted with some functionalities to achieve desired properties. Examples are amino-functionalized siloxanes and various alkyl modified silicones. Amino-functionalized siloxanes give better substantivity property due to interaction of amino groups with other polar materials such as proteins on the contact surface. Phenyl modified silicones are used as luster-enhancing additives in hair products since the phenyl groups on silicone chain increase the refractive index of the polymer. Also available are specialty materials containing a wide range of functionalities grafted onto the silicone chain, including protein moieties, fatty acids, amphoteric surfactants, amino acids, and fragrance oil.

In summary, although OMC is the most popular sunscreen in cosmetic industry nowadays, it still possesses a few problems including absorption through human skin and the photounstability. A few methods have been proposed to reduce skin penetration of sunscreen.<sup>27-29</sup> These include increasing viscosity of cosmetic formulations, using solid lipid microspheres (SLM) as carriers for the UV filters and using chemical modifier in the formulations.<sup>27</sup> These studies investigated the use of OMC molecules in modified formulations or carriers to minimize the skin penetration, however, transdermal permeation of the sunscreens cannot be totally blocked. We propose here the grafting of OMC absorption chromophore, 4-methoxycinnamoyl moiety, on silicone polymer to produce suncreening polymer that hopefully can be effectively retained on skin surface. Moreover, the problem on photostability of OMC should be reduced since the grafted chromophore will then be retained in more hydrophobic environment of silicone polymer.

#### **1.8 Research goal**

The objectives of this research can be summarized as follows:

- 1.8.1 To graft the UV filter chromophore; 4-methoxy cinnamic acid onto silicone.
- 1.8.2 To determine absorption wavelength, molar absorptivity, photostability and skin absorption of products.

ศูนย์วิจัยทรัพยากร  
จุฬาลงกรณ์มหาวิทยาลัย