

GENERAL ASPECTS OF PHOTOCHEMISTRY TO HUMAN

ASPEK UMUM FOTOKIMIA TERHADAP MANUSIA

Achmad Mursyidi

Dept. Pharmaceutical Chemistry, Faculty of Pharmacy,
Gadjah Mada University

ABSTRAK

Fotokimia, studi tentang reaksi kimia yang distimulasi oleh cahaya sangat besar perannya bagi kehidupan manusia. Reaksi fotokimia diawali oleh absorpsi cahaya menghasilkan molekul tereksitasi. Bergantung pada struktur molekul dan lingkungan molekul tereksitasi akan mengalami berbagai macam reaksi kimia.

Beberapa reaksi fotokimia berlangsung pada tubuh manusia dan sangat penting bagi kehidupan, misalnya peristiwa penglihatan (vision), pembentukan vitamin D, dan pengobatan psoriasis. Namun, ada pula reaksi fotokimia yang sangat merugikan misalnya penuaan dini kulit, kanker kulit, dan kerusakan kornea.

Fotosintesis dan fotodegradasi pestisida merupakan contoh reaksi fotokimia di lingkungan yang memberikan banyak manfaat bagi manusia. Sementara itu konsep fotokimia banyak digunakan untuk sintesis obat, nilon dan alkan-sulfat (detergen). Selain itu ada beberapa reaksi fotokimia yang tidak dikehendaki misalnya terbentuknya kabut fotokimia, penipisan lapisan ozon, dan degradasi obat. Berbagai aspek yang menguntungkan maupun yang merugikan bagi kehidupan manusia diuraikan dalam artikel ini.

Kata kunci: fotokimia, molekul tereksitasi, fotooksidasi, fotodegradasi, fotosintesis.

ABSTRACT

Photochemistry, the study of chemical reaction initiated by light plays an important role to human lifes. Photochemical reaction is intiated by the absorption of light giving excited molecules. The excited molecules, depending upon their structures and environment, may undergo various chemical reactions.

Some very important and beneficial photochemical reactions occur in human body such as photochemical reaction of vision, the formation of vitamin D, and psoriasis medication. On the other hand, some photochemical reactions result in harmful effect to human, for examples, skin ageing, skin cancer, and cornea damage.

Photosynthesis and photodegradation of pesticides are examples of photochemical reaction in the environment which are beneficial to human ienterset. In addition photochemical concept has been employed to synthesise drugs, nylon, and alkane-sulphates (detergents). However, some photochemical reactions create problem in the environment, i.e., formation of photochemical smogs, ozon layer depletion, and photodegaradion of drugs All those aspects of photochemistry are illustrated in this article.

Key words: photochemistry, excited molecule, photodegradation, photooxidation, photosynthesis.

INTRODUCTION

Photochemistry is the study of chemical reactions initiated by light. Phenomena concerning photochemical processes have been known for a long time but only in the last forty years has this subject been given serious and systematic attention.

The growth of photochemical knowledge started in the end of eighteenth century when Hales introduced photosynthesis. Since then, photochemistry developed sporadically particularly in countries having bright skies such as around the Mediteranean. In early twentieth century Ciamician and Silber reported from Bologna the results of their experiments demonstrating that sunlight could bring about some

remarkable transformation in organic molecules. About forty years later Schonberg and Mustafa discovered dimerization, abstraction, and cycloaddition reactions by light.

The development of the quantum theory in the late 1920s had a significant effect particularly in rationalizing interaction between light and molecules. Despite the development in theory, the study of photochemistry was only slowly progressing because of the unavailability of sufficient ultraviolet sources and inadequate methods of analyzing unusual and often complex product mixtures.

Light or electromagnetic radiation can be considered as a wave form following the relationship : $c = h\nu$, where c is the velocity of light (2.9979×10^8 m/sec), h is Planck constant (6.6256×10^{-34} J/sec.), and ν is frequency of radiation.

On the other hand, light can also be regarded as discrete quanta (photons) that can be expressed as : $E = h\nu = hc/\lambda$, where E is the energy of radiation and λ is the wavelength. This expression indicates that the amount of energy available is inversely proportional to the wavelength. The longer the wavelength the lower the energy of radiation, and vice versa.

With regards to the energy of radiation available and to the bond strength of molecules, particularly organic molecules, the region of electromagnetic spectrum which is of interest are the ultraviolet (200 – 400 nm) and visible (400 – 700 nm) region. Human body is in fact consisting of organic molecules, therefore, ultraviolet and visible light irradiation may directly initiates photochemical reaction on the body surface.

When a molecule is irradiated with light, absorption of energy may occur, where the amount of energy absorbed is depending upon the wavelength. The absorption of energy resulting in excitation of the molecule to a higher energy level. Excitation may occur in rotational, vibrational or electronic levels depending on the energy absorbed. Absorption of energy in the far infra red region, for example, causes rotational excitation levels, while excitation of vibrational energy levels which require more energy, occur in the infra red region of the spectrum.

Excitation of electronic energy levels, on the other hand, may take place when a molecule absorbs energy in the visible or ultraviolet region of the spectrum. The excited molecule possessing excess energy is reactive but unstable and tends to return to the ground state level (S_0). There are two kind excited states, i.e. singlet (S_1) and triplet (T_1) excited states. The average life time of singlet excited state is 10^{-9} to 10^{-5} seconds, while that of the triplet state is 10^{-5} to 10^{-3} seconds. The longer life time of triplet excited state is an important property that enable redistribution of energy within the molecule, a process which leads to the formation of active species. The fate of the excited molecule is very much depending on the environment and on the nature of the molecule.

In the case of absorbed energy is greater than the bond dissociation energy, chemical dissociation may occur. For instance, if absorption of radiation occurs at 250 nm (most common artificial ultraviolet light sources) the energy associated with this absorption calculated using the formula described above, is 480 kJ per mole. This is greater than the bond dissociation energy of carbon-carbon sigma bond ($D = 347$ kJ per mole). It is not surprising, therefore, the chemical reaction can be induced by uv-light. In the same way, it can be rationally understood that photochemical reaction can be induced by visible light.

As has been mentioned that the excited molecule tends to return to the ground state, a process known as deactivation. Basically there are 5 processes of deactivation.

- (i) Non-radiative deactivation where the excited molecule loses the energy via internal conversion, intersystem crossing, and vibrational cascade,
- (ii) Radiative deactivation where the excited molecule emits its excess energy in the form of light, known as fluorescence (S_1 to S_0) and phosphorescence (T_1 to S_0),
- (iii) Dissociation, where the excited molecule forms free radical followed by atomic bond cleavage, to give new molecule,
- (iv) Chemical reaction, where the excited molecule attacks ground state molecule to give new molecule, and
- (v) Energy transfer, where the excited state molecule transfer its excess energy to the ground state molecule to yield new excited molecule.

Energy transfer is very important process in the environment that enable chemicals (e.g. pesticides) which naturally do not absorb energy at the visible light region but experience photochemical degradation

under the influence of sun light. Energy transfer is also important in the formation of singlet oxygen, a reactive species which is very important in photosensitized oxidation.

PHOTOSYNTHESIS

One important basic need for human life is food particularly carbohydrates. The carbohydrates can be considered as the most important and largest photochemical reaction, known as photosynthesis. Photosynthesis is the reaction between water and carbon dioxide under the influence of sunlight. It is estimated more than 2×10^{11} ton of carbohydrates yielded every year (Coyle, 1985).

Photosynthesis occurs in the chloroplast being rich with chlorophyll a and b, and carotenoides. Chlorophyll a absorbs light radiation at > 680 nm (red) while chlorophyll b absorbs light radiation below 680 nm with maximum absorption at 650 nm and 480 nm. In addition, carotenoides absorbs yellow and green light not being absorbed by chlorophyll. This means that nearly all of sunlight radiations are absorbed by chloroplast.

The absorption of light induces the formation of excited chlorophyll molecule which in turn release its electron to give chlorophyll cation. The electron transfer takes place in such a way involving species of electron carrier 8-plastoquinone, cytochrom b (959), and plastocyanin. In this process a series of redox reactions take place i.e. oxidation of ADP into ATP, oxidation of water to give oxygen, and reduction of NADP⁺ (Nicotemide-Adenin-Dinucleotide-Phosphate) to produce NADPH. ATP and NADPH involve in the reduction of carbon dioxide to give mono saccharide phosphate that undergoes further enzymatic reactions yielding carbohydrates as human energy source.

HUMAN VISION

A photochemical reaction directly experienced by human is human vision. The key to the chemistry of vision is the availability of a light sensitive pigment known as rhodopsin, a Schiff base formed between 11-cis retinal and protein called opsin. When absorption of light occurs rhodopsin excites resulting in the formation of all trans retinal and opsin. The dissociation is not direct but involves many intermediates i.e. batorhodopsin, lumirhodopsin, metarhodopsin I, metarhodopsin II, and finally all-trans retinal and opsin. It is suggested that a small electric potential emitted during the conversion of metarhodopsin I to metarhodopsin II activate the nervous system (Honig, 1978) that enable human to see an object.

All-trans retinal and opsin are enzymatically converted to reform rhodopsin that enable the vision cycle to take place. This direct enzymatic conversion is catalysed by an isomerase enzyme. It might be appropriate to note that the Noble Prize was awarded to Prof. George Wald from Harvard University for his detail study of photochemistry of vision.

FORMATION OF VITAMIN D₃

A beneficial aspect of photochemical reaction is the formation of vitamin D₃. This reaction takes place on body surface where under the influence of direct uv irradiation of sunlight 7-dehydrocholesterol undergoes photoisomerisation via ring cleavage to give vitamin D₃. This phenomena misleads common people to conclude that sunrays contains vitamin D. It is important to state that such photochemical reaction has been employed to enrich vitamin D₃ content of fish oil by irradiation of the oil containing 7-dehydrocholesterol beside vitamin D₃.

PHOTOTHERAPY

Photochemical reaction has long been used for medication known as phototherapy. Psoralene, for example, has been used for curing psoriasis (Lokshmiopathi *et al.*, 1977). Psoralen is orally given to the patient followed by irradiation with artificial light source. The irradiation induces photoaddition reaction between psoralene and pirimidin ring in the nucleic acid to give cycloadduct disturbing cell division.

With regards to the possibility of photochemical changing of chemical in human body phototherapy has also been applied for neonatal jaundice where blood bilirubin concentration in prematur born baby is very

high. Under the influence of uv or blue light irradiation, bilirubin is photooxidized to give a non-toxic compound which is easily excreted. In this process an energy transfer is involved to yield singlet oxygen which in turn oxidize bilirubin to produce non-toxic product (Bonnet and Stewart, 1975).

SKIN CANCER

Apart from the beneficial aspects of photochemistry direct uv light irradiation shows adverse reaction to skin. It is widely known that radiation of uv-B (320 – 290 nm) may cause sunburn, skin ageing, and skin cancer. The degree of negative effect is very much depending upon the length and intensity of irradiation and of the nature of the skin. The coloured skin is less sensitive compared to that of the colourless skin. This is because the coloured skin has enough melanin to absorb uv irradiation.

The adverse effect of sun light irradiation relates to photooxidation of tryptophan and disulphide (S-S) bond cleavage. More serious effect usually involves chemical changing of the nucleic acid and protein associated with it (nucleoprotein).

Recent study on the photostability of cynamates and PABA, two compounds widely used in sunscreen preparation indicated that these two compounds were photolabile with half life was less than 3 hours (Astuti, *et al.* 1996). It means that applying such sunscreen during sunbathing does not guaranty from adverse effect of sunlight radiation.

Basically there are two important mechanisms involved in the development of skin cancer (Wang, 1976), i.e. photohydration and photodimerisation. Skin is relatively permeable to light, consequently penetration of light reaches 40% (Cornelison, 1980). Absorption of energy will be rapidly transferred to molecule possessing lowest triplet energy (pyrimidin and thymine). In the case of photohydration, the excited pyrimidin gives biradical followed by addition reaction with water at position C₅-C₆ to produce hydrate. As a result, mutation and changing property of RNA occur. In addition, photoaddition reaction can also take place with cysteine.

Photodimerisation reaction, on the other hand, takes place at thymine group to form cyclobutane-thymine dimer causing hydrogen bond between strand of the DNA breaks. Consequently, cell mutation happens. Other mechanism resulting in cell mutation is the photodimerisation of cytosine. In this case absorption of light energy induces the excitation of cytosine which in turn dimerizes followed by deamination. As a consequence cell mutation is not avoidable and skin cancer appears.

Other adverse effect of photochemical reaction is the damage of cornea and eye lens. Cornea damage is due to photochemical changing as illustrated above while lens damage is caused by photooxidation of tryptophan residue in the protein structure. This mechanism is based on the fact that tryptophan is an amino acid having the lowest triplet energy in the protein structure. Consequently, absorption of energy easily results in excitation of tryptophan moiety followed by the cleavage of double bond at C₂-C₃ to give N-formylkynurenin. The cleavage of the tryptophan moiety is not easily repaired because metabolism activity in the eye is very low. It is necessary to note that the chemical photooxidation increases in line with the increase of photooxidants (photochemical smogs) in the atmosphere.

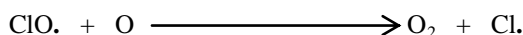
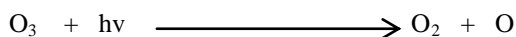
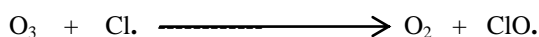
PHOTOCHEMICAL REACTION IN THE ENVIRONMENT

Photochemical processes in the environment plays an important role to the quality of human life. On the one hand it benefits to human as photochemical reactions take place in the environment help to clean the environment from the hazardous pollutants but on the other hand they also produce toxic chemicals.

An important example of photochemical reaction becoming a big concern among the environmentalist is the depletion of ozone layer. It is widely known that fluorine containing substances (freon or chlorofluorocarbon abbreviated as CFC) used as propellant in spray preparation and in air conditioning are very stable. They slowly undergo photochemical reaction at the ozone layer under the influence of uv radiation from the sun.

CFC's experience photodecomposition by the action of high energy of uv radiation to produce chlorine radical which in turn attacks ozone molecule to yield chlorine-oxide radical. The reaction continues as a chain reaction and depletion of ozone layer occurs. As a result the intensity of uv radiation from the sun reaching earth surface increases with a consequence of increasing skin cancer incidence.

The chain reaction causing ozone layer damage can be illustrated as the following.

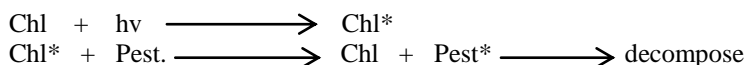


The chlorine radical will attack further ozone molecule causing further damage of ozone layer.

PHOTODEGRADATION OF PESTICIDES

The continuous introduction of pesticides to protect crops during growth, harvesting, and storage has created a serious environmental problems. One important route of disappearance of pesticides from the environment is photodecomposition. As most pesticide molecules naturally do not absorb radiation of visible region the most possible mechanism is energy transfer, where an absorbing molecules (usually coloured compounds) plays a determining role.

Dieldrin and 2,4-dichlorophenoxy acetate, for examples, which absorb uv-light energy at 215 nm and 230 nm respectively, undergo photodecomposition in the environment where the shortest electromagnetic radiation from the sun reaching earth surface is 290 nm. The photodecomposition, therefore, can only be explained via energy transfer from a sensitizer available (chlorophyll). In this regards, Crosby and Wong (1977) proved that dioxines herbicides underwent photodecomposition much faster on leaf surface compared to that of soil surface.



In the presence of oxygen an energy transfer from a sensitizer may produce singlet oxygen. The singlet oxygen species is very reactive to oxidize various kind of molecules included pesticides. This oxidizing process is known as sensitized photooxidation.

An interesting finding on the stability of DDT was reported by Mustafa *et al.* (1989) where half life of DDT in tropical soil was only three month. This report was very different from the literature showing the life time of DDT in the environment is more than ten years. This is because most of the data written in the literature obtained from area where the intensity of sun light is relatively low. As has been widely understood the rate of photochemical reaction is largely determined by the intensity and the angle of incidence light.

In line with the above finding, DDT was reported rapidly degraded when irradiated with light under the presence of a sensitizer (chlorophyll, rose bengal, or methylene blue). It is suggested that the sensitizer work in two ways : (i) the excited sensitizer molecule transfer its excess energy to DDT which then decompose, (ii) the sensitizer transfer its excess energy to oxygen to yield singlet oxygen. The singlet oxygen then oxidizes DDT to give benzoic acid and other products.

More specific sensitized photooxidation are experienced by organosulphur pesticides (Crank and Mursyidi, 1990). Folpet, captan, and captafol, for examples, are very sensitive upon sensitized photooxidation to give sulphur and sulphur dioxide. All of the above mechanisms indicate the significance of photochemical processes in cleaning the environment from toxic compounds, particularly pesticides.

Recently there are also efforts to employ photochemical concept in accelerating the decomposition of plastic. Realising that sun light irradiation reaching earth surface is greater than 290 nm there should be sensitizer added to the plastic composition, such as carbonyl, hydroperoxide, and metal. The predominant process of plastic photodecomposition is photooxidation initiated by the formation of free radical (Cichetti, 1970). This is understandable as most plastics consist of polymer of unsaturated monomers which are very sensitive to oxidation reactions.

PHOTOCHEMISTRY OF DRUGS

Photochemistry has dual aspects on drug. On the one hand it can be used for synthesizing new molecules but on the other hand photochemical reactions may cause photodegradation resulting in inactive or even toxic compounds. Consequently there are medical preparation containing particular class of compounds have to be kept out of light, for examples vitamins, antibiotics, hormones, alkaloids, sulphonamides, and psychotropics.

Chlordiazepoxide (librium), a psychotropic widely abused in society, for example, undergoes photoisomerisation when irradiated with uv light to give oxasiridine which then decomposes to yield quinoxaline and benzoxadiazocaine. The two final products are phototoxic (Cornelison, 1980). It was also revealed that the photodecomposition was accelerated by glutathione.

Diazepam (Valium), another example of psychotropic, is also photolabile with diazepam ring as the active site. When irradiated with uv light (254 nm) the diazepam ring cleaves and undergoes further degradation to produce 7 new compounds, derivatives of benzophenone and quinazoline. It is necessary to note that the product of photodegradation is determined by wavelength of irradiation used. When irradiation is done at 300 nm only glycine and benzophenone derivate are produced.

It is interesting, however, the presence of nitro group at benzodiazepam ring change their photochemical properties. Nitrazepam (Mogadon), klonazepam (Rivotril), and flunitrazepam (Rohypnol) are photochemically stable in the presence of oxygen. However, they undergo photoreduction when irradiated with uv light under nitrogen.

Photolability of vitamins is widely known. Vitamins A, B, C, and E easily degrade when irradiated with uv and visible light with double bond as the active site. In addition, photodegradation of sulphonamides, antibiotics, and hormones have also been reported.

Apart from its deteriorating aspect, photochemical concept has also been employed in synthesizing drug molecules. Beside vitamin D₃ as has been previously mentioned, an anthelmintic ascaridol has been synthesized from terpinen irradiated with visible light in the presence of oxygen and a sensitizer (Clements, 1985). The same principle has also been applied for the synthesis of rose oxide (used in perfumery) by irradiating sitronelol with visible light in the presence of rose bengal as sensitizer.

Another example of photochemical synthesis of drug is the production of prostaglandin precursor. Epoxybicycloheptanone is converted into cyclic-acetal known as prostaglandin precursor when irradiated with uv light.

PHOTOCHEMICAL SYNTHESIS

A lot of human needs have to be produced in a large scale. In some cases photochemical process is simpler and easier to handle. For example, the production of cyclohexanone-oxim from cyclohexane. Under the influence of uv light cyclohexane will react with NOCl to give cyclohexanone-oxim which can be converted to caprolactam in the presence of sulphuric acid. Caprolactam is the monomer of nylon 6.

Photochlorination is another example of photochemical reaction of industrial scale. This process is used for the production of solvent 1,1,1-trichloroethane from 1,1,1-dichloroethane and the synthesis of insecticide gamexane from benzene. Photochlorination of dichloroethane is very effective and easily handled as it can be carried out in liquid condition and below 100 °C. Benzene is very stable, however, chlorination will take place when a mixture of benzene and chlorine is irradiated with uv-light.

One more example of photochemical process of human interest is the synthesis of alkane-sulphate largely used for detergent. Alkane is treated with chlorine and sulphur dioxide under the influence of light.

CONCLUSION

A lot of photochemical aspects have been illustrated. Photochemistry covers many areas of human interest, however, only small number of people pay attention in developing this knowledge. Basically the general aspects of photochemistry can be differentiated in two ways; (i) direct and indirect effect to human, (ii) beneficial and harmful effect to human.

Vision, formation of vitamin D, treatment of prenatal jaundice and psoriasis are examples of direct and beneficial effect to human. On the other hand, skin ageing, skin cancer and cornea damage are examples of direct hazardous effect of photochemical reaction to human.

Photosynthesis of carbohydrates, photodegradation of pesticides in the environment, photochemical synthesis of drugs, nylon, and detergents are some examples of indirect with beneficial impact to human life while ozone depletion, photodegradation of drugs, the formation of photochemical smogs are examples of indirect and harmful effect of photochemical processes in the environment.

REFERENCES

- Astuti, R., Mursyidi, A., and Sumarno, 1996, Photostability of Octylmethoxycynamate and Its Influence on the Photostability of Tryptophan, Konggres Ilmiah ISFI, 3-6 July, Semarang Indonesia.
- Bonnet, R. and Stewart, J.C.M., 1975, "Photooxidation of Bilirubin in Hydroxylic solvent", *J. Chem. Soc. Perkin I*, **3**, 224-231.
- Cichetti, O., 1970, Mechanism of Oxidative Photodegradation and of uv Stabilisation of Photoolefins, *Adv. Polym. Sci.*, **7**, 70
- Clements, A. D., 1985, Photochemistry in Commercial Synthesis, *Chem. Brit.*, 464-466.
- Cornelisson, P. J. G., 1980, Photochemical and Photobiological Activity of some 1,4-Benzodiazepin, Wesselink Drukwerk B. V., Sassenheim.
- Coyle, J., 1985, Light and Biological System, *Chem. Brit.*, 460-462.
- Crank, G. and Mursyidi, A., 1990, Photochemical Reactions of Thioamides, *J. Photochem Photobiol., A : Chemistry*, **53**, 301-310
- Crosby, D. G. and Wong, A. S., 1977, Photodecomposition of Herbicides, *Science*, **10**, 1419-1424.
- Honig, B., 1978, The Photochemistry of the Visual Process, *Ann. Rev. Phys. Chem.*, **29**, 33.
- Lokshmipathi, T. P., Gould, W., Mackenzie, L. A., Johnson, B. E. and Frain-Bell, W., 1977, Photochemistry in the Treatment of Psoriasis, *Brit. J. Derm.* **96**, 586-594.
- Mustafa, I. Y., Zayed, S. M., and El-Arab, A. E.; 1989, Studies on Dissipation and Degradation of DDT in Egyptian Soil under Field Condition, FAO Coordination Research Project, IAEA, Vienna.
- Wang, S. Y., 1976, *Photochemistry and Photobiology of Nucleic acids*, Academic Press, London.