

CHAPTER II

LITERATURE REVIEW

Polymers, or macromolecules, are very large molecules formed by linkages of many smaller molecules, which are referred to as constitutional units or monomers. Plastics are polymeric materials which, at some point in their manufacture, can be shaped by heat, pressure, or both. There are many polymers, such as cellulose, which are not plastics are polymers.

Plastics used in packaging can be divided into two broad groups on the basis of structure and the bonding mechanism between the macromolecules (Figure 2.1). First, plastics whose macromolecules have linear or branched chains are called thermoplastic. They, once formed, can be melted and formed again. There are another group of plastics in which the individual molecules are bonded to another by cross-link. Plastic based on highly cross-linked molecular chain are called thermoset that can not be melted or reshaped by using heat and pressure.

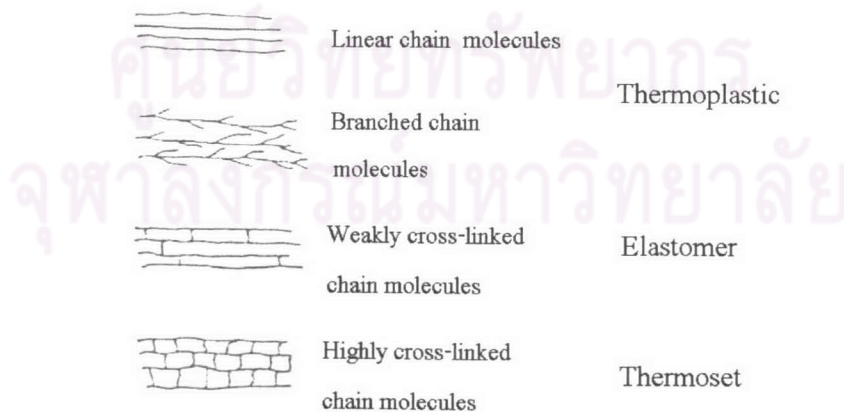


Figure 2.1 Illustration of the arrangement of chain molecules in plastic [2]

Polyethylene is probably the thermoplastic you see most in daily life. Polyethylene is the most popular plastic in the world and is widely used in Thailand. About 60% of all plastics used in packaging in USA are polyethylene. This is the polymer that makes grocery bags, shampoo bottles, children's toys, and even bullet proof vests. For such a versatile material, it has a very simple structure, the simplest of all commercial polymers.

2.1 Low density Polyethylene (LDPE)

Polyethylene was first produced in the laboratories of Imperial Chemical Industries, Ltd (ICI), England [1]. The first commercial ethylene polymer was branch polyethylene commonly designed as low-density polyethylene (LDPE). A molecule of polyethylene is nothing more than a long chain of carbon atoms, with two hydrogen atoms attached to each carbon atom, as shown in Figure 2.2.

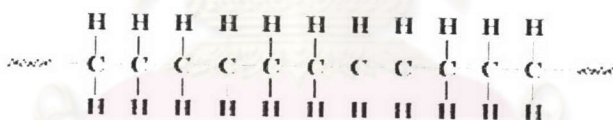


Figure 2.2 Polyethylene structure

Sometimes some of the carbons, instead of having hydrogen attached to them, will have long chains of polyethylene attached to them. This is called branched, or low-density polyethylene, or LDPE, as shown in Figure 2.3.

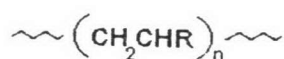


Figure 2.3 Low-density polyethylene structure

where R may be -H, $-(CH_2)_mCH_3$ or more complex structure with sub-branching

The mechanical properties of LDPE are between those of rigid materials like polystyrene and limp plasticized polymer like the vinyl. LDPE has a good toughness. At room temperature, LDPE is fairly soft and flexible material. It can maintain this flexibility well under cold condition, so is applicable in frozen food packaging. However, at moderated temperature, e.g., 100 °C, it becomes too soft for many uses.

The electrical properties of LDPE are outstanding. In thick section it is translucent because of its crystallinity, but high transparency is obtained in thin film. It is very inert chemically. It does not dissolve in any solvent at room temperature, but it is slightly swelled by liquids such as benzene and carbon tetrachloride which are solvents at high temperatures. It has good resistance to acids and alkaline, so it is often used as containers for acids. It is non-polar nature that makes it a relative good barrier against water vapor. Properties of LDPE are shown in Table 2.1.

Table 2.1 Typical properties of Low-density Polyethylene [15-16]

Properties	Value
Glass transition temperature (°C)	-120
Melting temperature (°C)	105 – 115
Decomposition temperature (°C)	340 – 440
Density (g/cm ³)	0.912 – 0.925
Tensile strength (MPa)	8.2 – 31.4
Tensile modulus (MPa)	55.1 – 172
Elongation at break (%)	100 – 965
Tear strength (g/25µm)	200 – 300
Impact strength, Izod (ft/b/in notch)	>16
Water absorption (%)	<0.01
Flammability	Burn with blue flame

LDPE is the most widely used packaging polymer, according to about one-third of all packaging plastics in the USA [2]. LDPE, whether used alone, blended, or in coextruded combinations with other members of the PE resin family, is a major factor in a variety of packaging, construction, agricultural, industrial, and consumer market application. The largest single outlet of LDPE is film (12 mils and below), which accounts for over 55% of the total volume of LDPE consumed domestically. Films made with LDPE exhibit good optics, strength, flexibility, low taste and odor transfer properties, and chemical inertness. Films are found application in the packaging of snack food, durable consumer goods, bakery items and industrial items. It is also used in non-packaging film areas such as disposable diapers, agricultural film and shrink film.

2.2 Polymer Degradation [3, 4, 5]

The apparent extent importances of degradation are subjective and largely determined by the use of the material. For polymer, degradation is frequently associated with chain cleavage and a drop in molecular weight. However, in some case, cross-linking reaction can render a polymer brittle, whereas in other case color generation is often objectionable but need not necessarily be accompanied by backbone scission.

Bond scission is frequently the process of overwhelming practical importance in polymer degradation. Many energy sources can cause this scission, as shown in Figure 2.4. In addition, the bond scission can result from exposure of the polymer to shearing, grinding, and other mechanical working.

In board terms, degradation usually involves the chemical modification of the polymer by its environment, modification that is often (but not always) detrimental to the performance of the polymeric materials. Although the chemical alteration of the polymer is frequently a destructive process, for some applications degradation can be controlled and

encouraged to achieve a specific property. Examples include the adjustment of the molecular weight of a thermoplastic in the extruder through controlled backbone scission, and the controlled oxidative cross-linking of surface coating. Embrittlement induced by weathering is a technologically successful way to destroy modified plastic film, either in the form of litter or agricultural mulch.

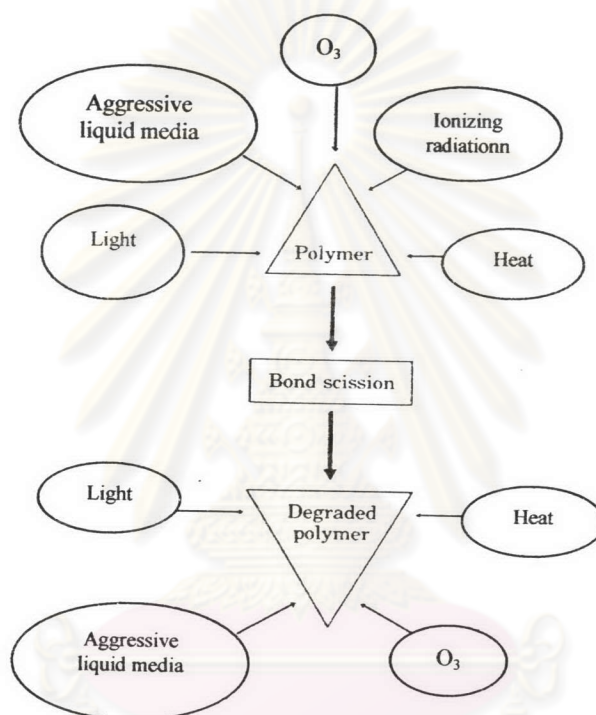


Figure 2.4 Sources of degradation and their interrelationship [4]

2.3 Modes of Polymer Degradation

It is useful to subdivide polymer degradation into 5 groups according to its various modes of initiation as follows:

1. Chemical Degradation refers to process which are induced under the influence of chemical (e.g. acids, bases, solvents, reactive gases, etc) brought in to contact with polymers.
2. Thermal Degradation refers to the case where the polymer, at elevated temperature, starts to undergo chemical change without the simultaneous involvement of another compound. Often, it is rather difficult to distinguish between thermal and thermo-chemical degradation because polymeric materials are rarely chemically pure. Impurities or additives present in the material might react with the polymeric matrix, if the temperature is high enough, causing thermo-chemical degradation.
3. Biodegradation is strongly related to chemical degradation as far as microbial attack is concerned. Microorganisms produce a great variety of enzymes which are capable of reacting with natural and synthetic polymers. The enzymic attack of the polymer is a chemical process which is induced by microorganism in order to obtain food (the polymer serves as a carbon source). The microbial attack of polymer occurs over a rather wide range of temperatures.
4. Mechanical Degradation generally refers to macroscopic effects brought about under the influence of a variety of modes of shear and stress forces such as machining (grinding, milling, process extruders etc.) or modifying process (cutting, drilling, free-cutting machining etc.). Strain is also frequently imposed on to the polymers when plastic articles are subjected to tensile or shear forces.
5. Photodegradation (or Light-induced degradation) concerns the physical and chemical change caused by irradiation of polymers with ultraviolet or visible light. The importance of photodegradation of polymer derives from the fact that the ultraviolet portion of the sunlight spectrum can be absorbed by various polymeric materials. The resulting chemical process may lead to severe property deterioration.

The strong inter-relationship between the various modes of polymer degradation should be emphasized. Frequently, circumstances permit the simultaneous occurrence of the various modes of degradation. Typical examples are: (a) environmental process, which involve the simultaneous action of UV light, oxygen and harmful atmospheric emission or (b) oxidative deterioration of the thermoplastic polymers during processing, which is based on the simultaneous action of heat, mechanical force and oxygen.

2.4 Theory of Photodegradation

Sunlight was soon recognized as an important factor in the deteriorative ageing and weathering processes which occur in commercial polymer [5]. The reasons for this are readily understood. The wavelength of the radiation from the sun which reaches the earth's surface extends from the infrared (>700 nm), through the visible spectrum (approximately 400-700 nm) in to the ultra-violet (<400 nm) with a cut-off at approximately 300 nm depending upon atmospheric conditions. The sunlight spectrum is shown in Figure 2.5

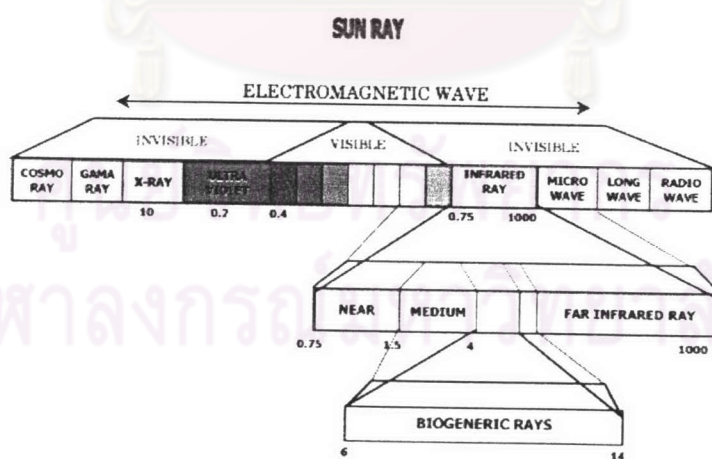


Figure 2.5 A spectrum of sunlight (\AA unit)

The energies of 700-400 and 300 nm photons are approximately 170, 300, and 390 kJ mol⁻¹, respectively. The strengths of C-C and C-H bonds are approximately 420 and 340 kJmol⁻¹, respectively although they may be very much less in certain environments, for example in the neighborhood of aromatic or unsaturated structures. Thus, it is clear that the energy of the quanta of the UV and possibly of the visible components of sunlight is sufficient to break chemical bonds and that the shorter wavelengths will be the most effective.

Of course, it is not enough that sufficiently energetic quanta are available. Chromophoric are necessary to absorb the incident radiation. In polymer, these are usually unsaturated structures such as carbonyl, ethylenic, or aromatic groups. The absorption of energy and its transfer to the bond to break may be described as the photophysical aspect of photodegradation.

The first chemical step in photo-degradation is usually homolytic bond scission to form free radicals. These radicals will normally react rapidly with any oxygen present. In this way, visible and especially UV radiation are particularly effective initiators of oxidation.

Only absorbed rays can cause photochemical changes. Thus, the UV absorption spectrum of a polymer is critical in determining its photosensitivity. Polymer has different photodegradative sensitivities to UV light of different wavelengths [4]. The varying sensitivities result from differences in the chemical structure. As show on in Table 2.2, the maximum sensitivity of several polymers (as determined by the bond dissociation energies) is in the range of 290 and 400 nm. Obviously, aromatic polymers absorb at longer wavelengths than fully aliphatic resins, but Table 2.2 can only be taken as rough guide to sensitivity to solar radiation because polymers are seldom free from trace impurities that may be highly efficient sensitizers. Although the atmosphere of the earth filters out the UV part of solar radiation, the range of solar ultraviolet radiation is about 6 % of the total radiation of the sun which reaches the earth's surface.

Table 2.2 Wavelength of UV radiation (energy of photon) at which various polymers have maximum sensitivity and weathering lifetimes of common polymers [4]

Polymer	Wavelength (nm)	Outdoor lifetime ^a (year)
Polycarbonate	295,345	0.5
Polyethylene	300	0.5-1.0
Polystyrene	318	0.1 ^b
Poly(vinyl chloride)	320	0.5
Polypropylene	370	0.2

^a 10 μm film. Unstabilized grade, normal impurity levels. Time to ~50% loss in tensile, elongation, or impact properties.

^b Yellowing.

2.4.1 Photo-physical processes

The physical processes involved in photodegradation include absorption of light by the material, electronic excitation of the molecules, and deactivation by radiative or radiationless energy transitions, or by energy transfer to some acceptor [5]. When the lifetime of the excited state is sufficiently transformed.

Phenomenologically, the absorption of the light can be described by Beer-Lambert's Law, as given in equation 2.1. The intensity of the incident radiation (I_0) will be only partly transmitted (I) through the material; the logarithm of the transmittance ($T = I / I_0$), is proportional to the thickness of the layer (l) and to the concentration of the absorbing component (c):

$$A = -\log(T) = \log(I / I_0) = \epsilon lc \quad (2.1)$$

Where the proportionality factor is the absorption coefficient (ϵ). A (also known as the extinction, E) is a dimensionless; i.e., when l is given in cm and c in mol/liter, then the dimension of ϵ is liter mol⁻¹cm⁻¹ (molar absorption or extinction-coefficient).

The absorption of light results in an electronic transition between two energy levels in the absorbing molecule. This absorbed energy exactly equals to the energy of a light quantum:

$$\Delta E = h\nu \quad (2.2)$$

where h is Planck's constant and ν is the frequency of the absorbed light:

$$\nu = (c^*)/(\lambda) = (c^*)(\nu^*) \quad (2.3)$$

where c^* is the velocity, λ is the wavelength, and ν^* is the wave number of the absorbed light (a possible set of values and dimensions: $h = 6.62 \times 10^{-27}$ erg sec, $\nu \text{ sec}^{-1}$, $c^* = 3 \times 10^{10}$ cm sec⁻¹, λ cm, $\nu^* \text{ cm}^{-1}$).

The energy absorption produces an excited state of the molecule, two types of which can be distinguished. In a single state (S) the spins of the electrons are (remain) paired, in a triplet state (T) are unpaired. The ground state is almost always a singlet state (S_0). An excitation of a molecule from the ground state to the first excited singlet state ($S_0 \rightarrow S_1$) is shown in Figure 2.6. Here, the curves represent the potential energies of the corresponding state and the horizontal lines are the various vibrational energy levels. The excited molecule can lose its energy by vibrational relaxation and emission (fluorescence). Radiationless transition (internal conversion) from higher excited singlet state (S_2, S_3 , etc.) to the S_1 state, or from S_1 to the S_0 state is also possible.

A direct excitation from S_0 to an excited triplet state is not allowed. This transition is, however, possible by intersystem crossing, an example of which is shown in Figure 2.7. The condition of such a transition is that the potential curves of S_1 and T_1 have a common (crossing) point with identical nuclear configuration so that a vibrational transmission ($S_1 \rightarrow T_1$) is possible.

The radiative deactivation $T_1 \rightarrow S_0$ is also forbidden; therefore, the T_1 excited triplet state has a much longer lifetime than the S_1 state. The emission of light by $T_1 \rightarrow S_0$ transitions called phosphorescence

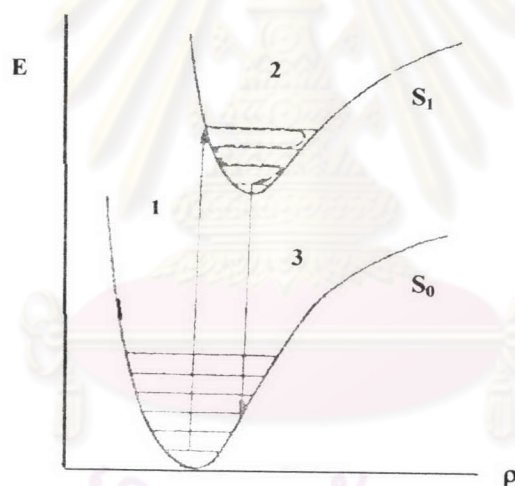


Figure 2.6 Potential energy curves of a molecule S_0 = ground state, S_1 = first excited single state : (1) absorption; (2) vibrational relaxation; (3) fluorescence [6]

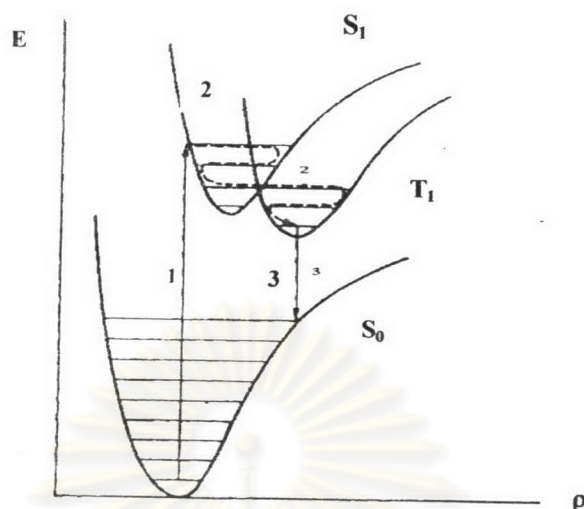


Figure 2.7 Potential energy curves of a molecule S_0 = ground state, S_1 = first excited single state, T_1 = first excited triplet state : (1) absorption; (2) inter-system crossing by vibrational relaxation; (3) phosphorescence [6]

2.4.2 Photo-Chemical Processes

The chemical processes of photodegradation include isomerization, dissociation, and decomposition of a molecule as a direct consequence of its photophysical excitation, as well as those nonunimolecular chemical reactions which are facilitated by the absorbed energy. Obviously, a photochemical reaction can take place only during the lifetime of the excited state; such as a reaction must complete with the physical modes of deactivation [6].

Photodissociation occurs when the excitation reaches a point above the dissociation limit of the excited potential curve, as illustrated in Figure 2.8a, or when a dissociative excited state is formed (Figure 2.8b) in which repelling of the atoms occurs at any separation distance. Dissociation can also occur after intersystem crossing to an

excited triplet state above the dissociation limit (Figure 2.9a) or to a dissociative potential curve (Figure 2.9b)

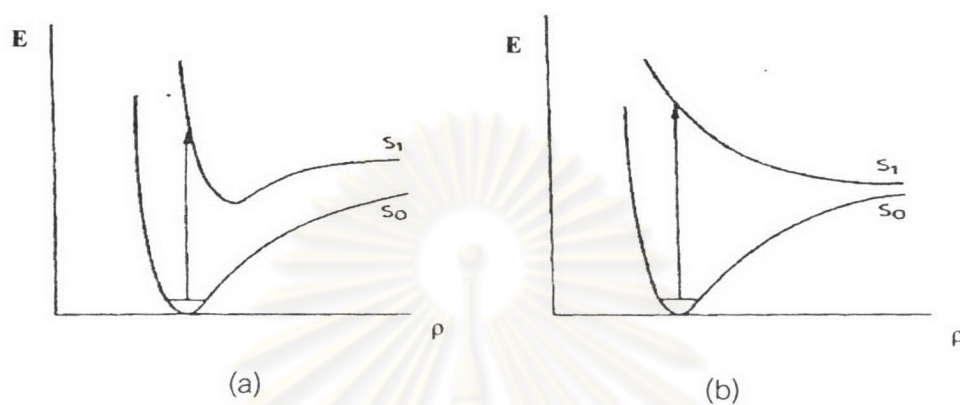


Figure 2.8 Photodissociation of the molecule: (a) by excitation above the dissociation limit of the S_1 potential curve; (b) by formation of a dissociative excited state [6]

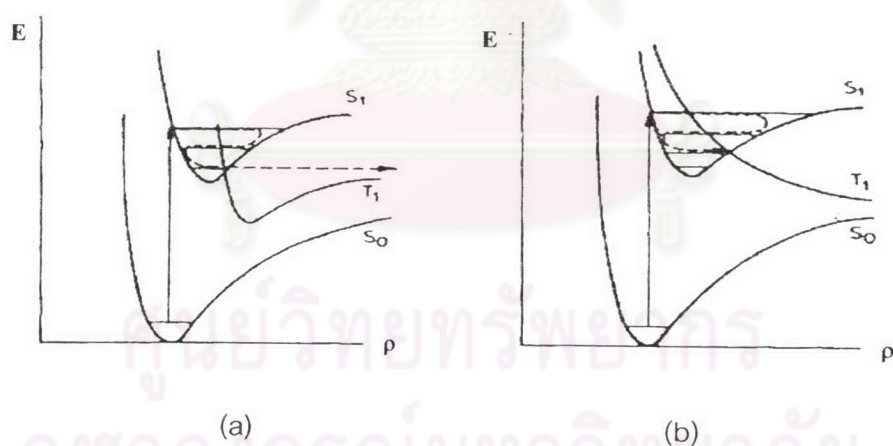
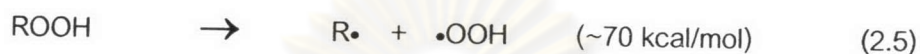
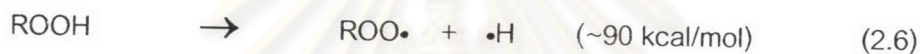


Figure 2.9 Photodissociation of the molecule after intersystem crossing: (a) above the dissociation limit of the T_1 potential curve; (b) to the dissociative excited triplet state [6]

An especially important case of photodecomposition is the radiation-induced decomposition of hydroperoxides formed during polymer oxidation. The energy of UV light is sufficient to cause both of the following decomposition:



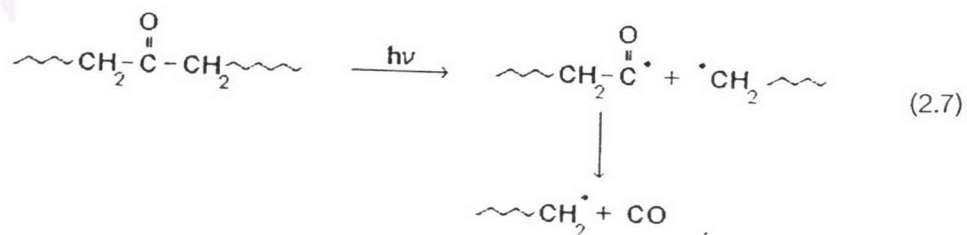
Dissociation of the O-H bond is less facile:



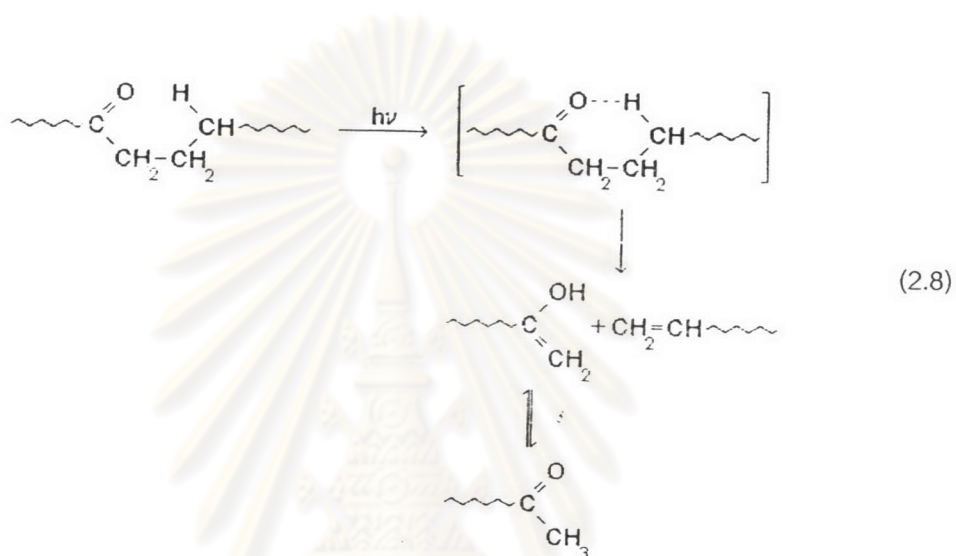
Because of low bond dissociation energy, decomposition according to reaction (2.4) is predominant in polymer photooxidation.

The role of carbonyl groups in polymer photooxidation is of great importance because once they have been formed they absorb UV readily; hence excitation to singlet and triplet states is easy.

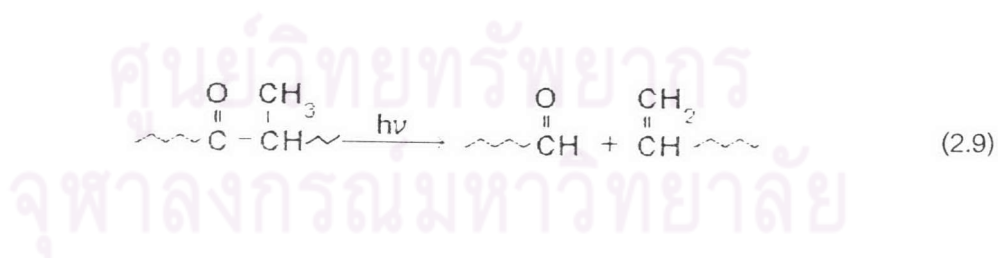
The excited carbonyl groups undergo cleavage of the bond between the carbonyl group and α -carbon atom (α -scission) and is usually followed by the formation of carbon monoxide. This reaction is called Norrish-I (2.7):



The Norrish-II reaction (2.8) is a nonradical scission which occurs through the formation of a six-membered cyclic intermediate in decomposition by β -scission to an olefin and an alcohol or ketone. For example, in the case of polyethylene, a terminal double and an enol/ketone end group are formed



The Norrish-III reaction (2.9) is also a nonradical chain scission; however, it involves the transfer of a β -hydrogen atom and leads to the formation of an olefin and an aldehyde:



The activation energies of the Norrish reactions are different; the probability of Norrish-II ($E_a = 0.85$ kcal/mol) is higher at room temperature than that Norrish-I ($E_a = 4.8$ kcal/mol); the latter is, however, more probable at higher temperature.

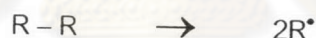
2.4.3 Photo-Oxidation

2.4.3.1 Autooxidation Processes

Plastic is a hydrocarbon polymer. When it is exposed to the radiation energy, chemical bond will break and begin to degrade. Effective degradation happens with the presence of oxygen. The first chemical step in photodegradation is usually a homolytic bond scission to form free radicals. These radicals will normally react rapidly with any oxygen presented and then form chemical groups, especially hydroperoxide group (ROOH). The hydroperoxide group will then decompose to carbonyl group and hydroxyl group, which is the importance case of plastic degradation. In this way, UV radiation is particularly effective initiator of oxidation.

The conventional mechanism of autooxidation is as follow [3]:

1. Hydrocarbon molecules break into free radicals.



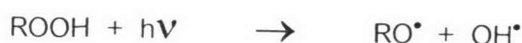
2. Hydrocarbon radical (R^{\bullet}) reacts with oxygen and form peroxide radicals (ROO^{\bullet}).



3. Peroxide radical accepts H atom from the other hydrocarbon molecule to generate hydroperoxide (ROOH).



4. Hydroperoxide groups are photolytically decomposed into alcoxy radical (RO^{\bullet}).



In Photooxidation the sample thickness is even more important than in thermal degradation. The extent of oxidation mainly occurs in very thin surface layer of the material.

Various chromophores originally presented in the polymer, accumulated during processing and storage, or added intentionally to the polymer may have an important effect on photostability. Metallic impurities, e.g., residues of Ziegler-Natta catalysts of metallic traces originating from processing equipment, may have a catastrophic effect because they can participate in various steps of photooxidation.

2.4.3.2 Sensitized and Additive-Initiated Degradation

It is clear that the energy of the quanta of UV light is sufficient to break chemical bonds. However, the ever-increasing amount of plastics used for disposable packaging material and their potential for causing permanent pollution of the environment have prompted workers to seek methods of producing polymer with controlled service life. After having finished its useful function, e.g., as a container for milk, the plastic becomes a waste material; it is desirable that this waste can be decomposed with the aid of sunlight, humidity, and bacteria as rapidly as possible.

The photodegradation of plastic can be enhanced by two basic ways. The first one is the introduction of a chromophoric group in the backbone of the polymeric chain during or after the polymerization process in comonomer form. Chromophoric groups are necessary to absorb the incident radiation. In polymer, these are usually unsaturated structures such as carbonyl, ethylenic or aromatic groups. These chromophores can give rise to the initiation of new chain reaction upon prolonged irradiation and thus to rapid deterioration of the polymer. Another way is adding or mixing low-molecular-weight chemical (so called photosensitizer) in the form of additive.

Recently, the term sensitization has been used by photochemists to solely donate process involving energy transfer which is subsequently followed by a chemical reaction or a physical process.

The mechanism of photosensitization is as follow [3] :

1. An additive absorbs radiation energy and turns into excited state



2. An excited additive can be transferred absorbing energy to polymer molecule



3. Excited polymer molecule will be separated into free radicals



These free radicals will react with any oxygen presented, leading to the reduction of polymer molecular weight.

Apart from that, an excited additive or photosensitizer can also be changed into free radicals by two routes.

1. Excited initiator molecules dissociating readily into free radicals after excitation or so called "intermolecular photocleavage"



2. Intermolecular hydrogen abstraction



These free radicals are the beginning of polymer degradation.

2.4.4 Photosensitizer

Photosensitizer or photoactivator is a compound which has a high absorption coefficient for UV light. The excited compound either decomposes into free radicals and initiates degradation or oxidation of the polymer, or transfers the excitation energy to polymer (or to oxygen). Many compounds have been studied for their photoactivity as shown in Table 2.3

A good sensitizer should be easily admixed with the polymer and must not decompose thermally.

Table 2.3 Compounds examined for photoactivity [6]

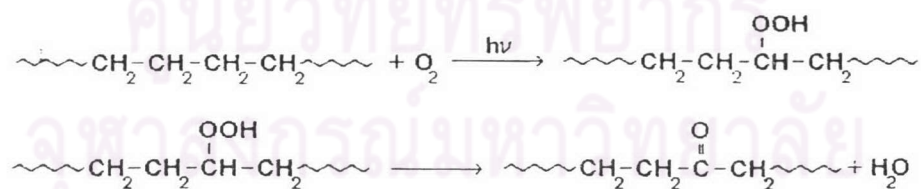
Compound	Photosensitizer
Aromatic Carbonyl Compounds	Deoxyanision, Flavone, 10-Thioxanthone Dibenzocycloheptadienone
Organosulfur Compounds	Benzyl disulfide, Phenyl disulfide 2-Mercaptobenzothiazole
Inorganic Pigments	Titanium dioxide, Zinc Oxide
Quinones	Anthraquinone Methoxyanthraquinone 2-Ethylantraquinone

Compound	Photosensitizer
Organo-metallic Compounds	Ferric octanote (1%) Manganous stearate
Transition Metal Salts	Copper Carbonate Manganous Chloride Ferrous Ammonium Sulphate
Aromatic Amines	4-4'-Methylenebis (n,N-dimethylaniline) Triphenylamine

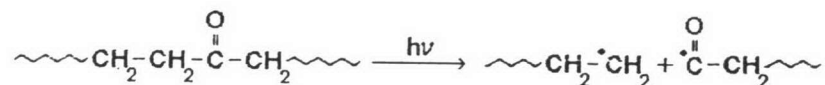
2.5 Photodegradation of Polyethylene

Polyethylene is relatively resistance to UV radiation in the absence of oxygen. However, when it is exposed to both oxygen and UV radiation it becomes brittle because of photooxidation. Hydroperoxide and carbonyl group are generated and then polyethylene molecule that contains carbonyl group will be dissociated by Norrish type I or Norrish type II reactions. These processes result in reduction in polymer molecular weight.

The mechanism of polyethylene photooxidation is shown in Figure 2.10



Norrish Type I



Norrish Type II

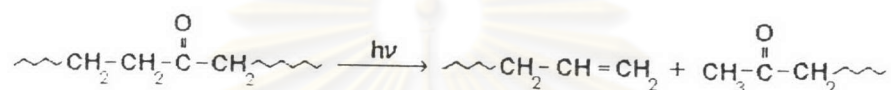
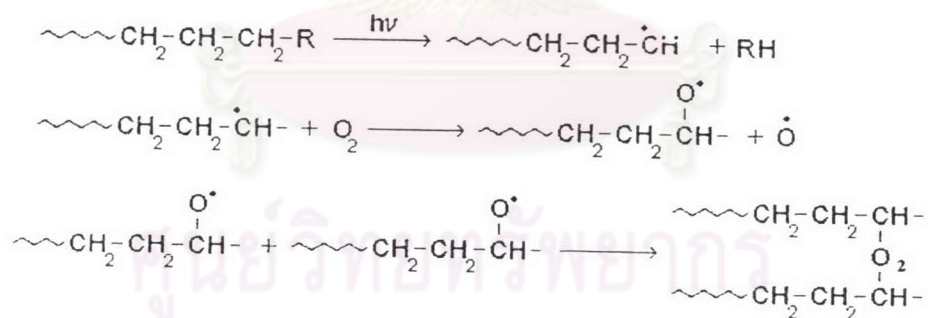


Figure 2.10 The mechanism of polyethylene photooxidation

Furthermore, crosslink reaction between polyethylene molecules can be occurred, as shown in Figure 2.11



or

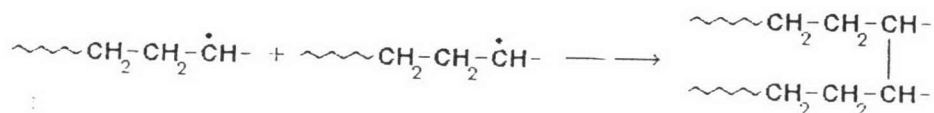


Figure 2.11 Crosslink reactions between polyethylene molecules

Many investigators studied the degradation of plastics in different ways. The works reported on the changes of artificial weathering and natural weathering with/or without introducing photosensitizers into the plastic. The physical, chemical properties and character of degradable plastics were observed. Some works were summerized as follow.

In 1981, L.J. Taylor and J.W. Tobias [9] studied the accelerated photo-oxidation of polyethylene. A number of additives observed to promote photo-oxidative degradation of PE films had been evaluated with respect to their ralative photo-initiating effectiveness at wavelengths near 300 nm. Depending on the nature of the additive, the photo-oxidation process may display autoretarding of autoaccelerating behavior. Thermomechanical analyses and gel content measurements on UV exposed films containing substituted anthraquinones suggest that at short exposure times, photo-oxidative degradation was accompanied by photochemical crosslinking

In 1990, A.L. Andrady [19] investigated the outdoor weathering of polyethylene (PE) homopolymer under exposure in air and in sea water. Photo-oxidative degradation of PE films as monitored by changes in the tensile properties, particularly the mean ultimate extension, was markedly lower when the samples were exposed outdoors, floating on the sea water, compared to those exposed in the air. The slower rates of degradation in the sea water were possibly due to the sample being maintained at a relatively lower and stable temperature in the sea water compared to those exposed in the air. However, the samples were embrittled in both cases.

In the same year, M. Raab et al. [20] investigated the degradation of LDPE film containing quinoid sensitizers, α -butylanthraquinone, 2-octanovloxyanthraquinone and anthraquinone. LDPE films were exposed to the UV light from fluoresent tube. The change in the tensile strength and IR absorptions were recorded during irradiation to control the undergoing processes in the LDPE films. The results showed that the quinoid sensitizer can cause the accelerated photo-oxidative degradation of LDPE film. The tensile strength

decreased proportionally to the exposure time and a faster decrease was observed as the sensitizer concentration increased.

In 1998, H. Kubota et al. [10] examined the effect of benzophenone on the photodegradation of polyethylene by analyzing the Electron Spin Resonance (ESR) and infrared spectra of the irradiated samples. Infrared spectra of the irradiated PE showed that benzophenone strongly accelerated the formation of double bonds. It is believed that benzophenone acted in the photodegradation of polyethylene to enhance the formation of ally and polyenyl radicals, which starts at the double bonds in the sample

In 2000, H. Kaczmarek [11] studied the influence of low-molecular organic compounds such as benzophenone (BPh), anthraquinone (AQ), and benzoyl peroxide (BPO) on the phototransformations of polystyrene. The viscometry, gravimetry, infrared and UV-vis spectroscopy have been used in these studies. The results indicate that additives applied accelerate and increase the efficiency of photodegradation, photodestruction and photo-oxidation process in polystyrene but they hamper the photocrosslinking and formation of double bonds in the polymer. In all these process, BPh showed the greater activity as photoinitiator comparing to AQ and BPO.

In 2003, H. Kaczmarek [25] modified polystyrene (PS) and poly(vinyl chloride) (PVC) by introducing 1-5 %wt addition of ketone (acetophenone or benzophenone) for the purpose of increasing degradability of polymer. The influence of UV radiation on the thin films of modified polymers was studied. These results show that the influence of both acetophenone and benzophenone upon the course of photodegradation and photo-oxidation is greater for PS than in case of PVC. However, both ketones induce efficient acceleration of reactions leading to the formation of chromophoric groups in UV-irradiated PVC.

2.6 Microencapsulation

Microencapsulation is a process of applying relatively thin coatings to small particles of solid or droplets of liquids and the products from this process are called microcapsules [7-8, 17-18]. The microcapsules developed for use in medicine consist of a solid or liquid core material containing one or more drugs enclosed in coating as shown in Figure 2.12. The core may also be referred to as the nucleus or fill and the coating as the wall or shell. Depending on the manufacturing process, various types of microcapsule structures can be obtained as illustrated in Figure 2.13. As shown, the most common type is the monomolecular spherical. Particle size of the microcapsules is defined in various ranges but can be varied from approximately 1 μm to 5,000 μm [7,18].

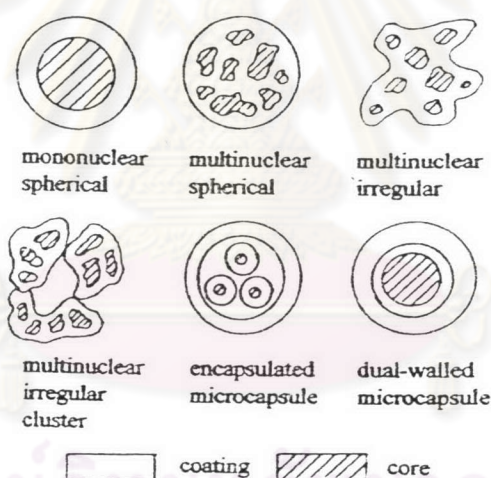


Figure 2.12 Some typical structures of microcapsule [17]

2.6.1 History of Microencapsulation Technique

The first research leading to the development of microencapsulation procedures for pharmaceuticals was published by Bungengerg de Jong and Kass in 1931 and dealt with the preparation of gelatin spheres and the use of gelatin coacervation

process for coating. In the late 1930s and 1940s, Green and co-workers developed the gelatin coacervation process to prepare carbonless carbon paper. The microcapsules, containing a colorless dye precursor (3,3-bis-(p-dimethylaminophenyl)-6-dimethylaminophthalide), were fixed to the under surface of the top page and released the dye precursor upon rupture by pressure from the tip of writing instrument. The liberated dye precursor then reacted with acidic clay (attapugite) on the top surface of the underlying page to form the copy image, dark blue color, as illustrated in Figure 2.13 [10].

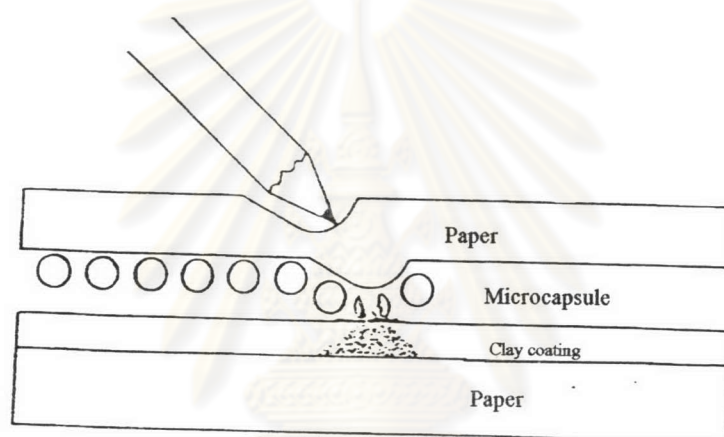


Figure 2.13 Pressure-activated release of encapsulated dye precursor to give a color reaction on paper coated with acidic clay.

2.6.2 Microencapsulation Procedures

Many microencapsulation procedures have been developed for the coating of pharmaceuticals. There are difficulties to classify simply under any one heading; however, they may be classified in to 3 major categories which are coacervation or phase separation, interfacial reaction, and miscellaneous mechanical methods [8]. These major microencapsulation procedures were briefly summarized in Table 2.4 [8, 18]. The

coacervation or phase separation using aqueous vehicles was used in this research and will be presented more details in next topic.

Table 2.4 Summary of microencapsulation procedures.

Process	Principle	Typed of core	Type of coating
1. Coacervation or Phase separation	Reduction in the solvation of polymeric solute(s) in a medium to form coacervate droplets to deposit and coat the disdersed phase	Vehicle-insoluble drug	Vehicle-soluble polymer(s)
2. Interfacial reactions	Reaction of various monomers at the interface between two immiscible liquid phase to form a film of polymer that encapsulated the dispersed phase	Water-soluble and water-insoluble monomers	High molecular weight materials such as enzymes and hemolysates
3. Miscellaneous mechanical methods 3.1 Air suspension	Polymer solution is spray-applied to the suspending and moving particles in the coating chamber of air suspension apparatus	Non-volatile and solid drug	Water-soluble or organic solvent-soluble polymer(s)

Process	Principle	Typed of core	Type of coating
3.2 Pan coating	Polymer solution is spray-applied to the desired solid core material, which is adhered on the spherical substrate e.g. sucrose pellets, in the coating pan while rotating	Non-volatile and solid drug	Water-soluble or organic solvent-soluble polymer(s)
3.3 Spray drying	Dispersing the core material in coating solution and then atomizing the mixture into a hot air stream to remove the solvent from the coating material	Solvent-insoluble drug	Solvent-soluble polymer(s)

Various microencapsulation procedures will give the different characteristic size ranges of microcapsules as shown in Table 2.5 [17].

Table 2.5 Microcapsule size range produced by various production procedures.

Production process	Size range (μm)
Coacervation / Phase separation	1-2,000
Interfacial polycondensation	2-2,000
Air suspension	50-1,500
Pan coating	200-5,000
Spray drying	5-800

2.6.3 Coacervation Procedures Using Aqueous Vehicles

Coacervation is a colloidal phenomenon. The term coacervate, from the Latin *acervus*, meaning a heap or aggregation, was first introduced into the scientific literature by two Dutch scientists, Bungenberg de Jong and Kruyt, to describe the flocculation or separation of liquids from solution when at least one of the liquids contained a macromolecular or colloidal solute [8,17].

Generally, this microencapsulation procedure consists of three steps carried out under continuous agitation, as shown in Figure 2.15.

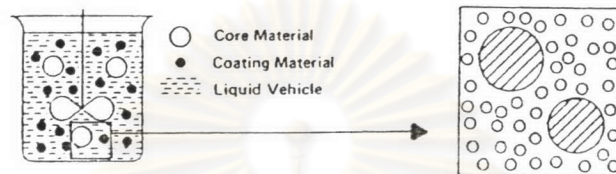
In step one; the three immiscible chemical phases are formed. The core material is dispersed in a solution of the coating polymer. The solvent for the polymer is the liquid manufacturing vehicle. The coating material, the immiscible polymer in the liquid state, is formed as coacervate droplets of colloid-rich phase by utilizing one of the methods of phase separation or coacervation, that is, by simple or complex coacervation, temperature change, addition of a nonsolvent, or polymer-polymer incompatibility.

In step two, the liquid polymer coating (coacervate droplets) is deposited around the core material by controlled physical mixing of the coating (while fluid) and the core material in the liquid manufacturing vehicle. Deposition of the liquid polymer coating around material occurs if the polymer is adsorbed at the interface formed between the core material and the liquid manufacturing vehicle. This sorption phenomenon is a prerequisite to effective coating. The continued deposition of the coating is promoted by a reduction of total free interfacial energy of the system which is brought about by a decrease in the coating material surface area during coalescence of the liquid polymer droplets.

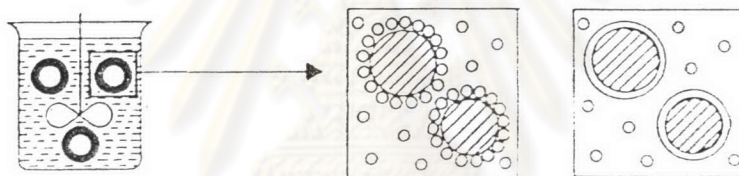
Step three of the process involves solidifying of the coating which is usually induced by thermal, cross-linking, or desolvation methods to form rigid microcapsules. The

desolvation can be performed by addition of non-solvent or phase-inducing polymer or by a change in pH.

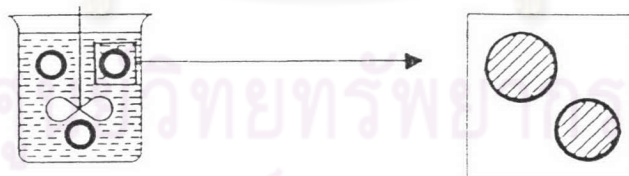
1. Establishment of three-phase system



2. Deposition of liquid-polymeric coating material



3. Solidification of coating material







( core,  coacervate droplets,  coating,  hardened coating)

Figure 2.14 General process description of coacervation technique

2.6.4 Type of Coacervation

Coacervation has been subdivided into two categories: simple coacervation and complex coacervation. Some basic characteristic features of the two systems are summarized in Table 2.6.

2.6.4.1 Simple Coacervation

Simple coacervation usually deals with systems containing only one colloidal solute. It is a process involving the addition of strongly hydrophilic substance to a solution of a colloid. This added substance causes two phases to form; one phase is rich in colloidal droplets and the other is poor in such droplets. This process depends primarily on the degree of hydration produced. For example, an addition of ethanol or sodium sulfate, as typical hydrophilic substances, to an aqueous solution of gelatin can lead to the two phases formation. When suitable conditions including the presence of suitable nuclei are prevalent, microcapsules may result.

Methanol, isopropanol, resocinol, acetone and any suitable organic liquids can be used instead of ethanol to cause a similar effect and various salts can be also used instead of sodium sulphate. Useful salts for coacervation may be made from the cations ($\text{Na}^+ > \text{K}^+ > \text{Kb}^+ > \text{Cs}^+ > \text{NH}_4^+ > \text{Li}^+$) and the anions ($\text{SO}_4^- > \text{citrate} > \text{actone} > \text{Cl}^-$), such being arranged in the order of their effectiveness in this process.

Table 2.6 Characteristic of simple and complex coacervation

Characteristics	Simple coacervation	Complex coacervation
1. Components needed	At least one must be a macromolecule, e.g. gelatin	Two polymers capable of carrying opposite charges, e.g. gum arabic / gelatin
2. Presence of charge on the macromolecules	Has no consequence in inducing coacervation	Determines whether or not coacervation will take place
3. Presence of salts	Promotes coacervation effectiveness follows the lyotropic series	Suppress coacervation position of ions in lyotropic series is of minor significance
4. pH of cocervation	Not of great significance (usually a very large margin)-also occurs at pH > isoelectric point of gelatin	Highly dependent on pH (usually a very narrow range)-also occurs at pH < isoelectric point of gelatin

Many researches have been studied on the simple coacervation technique. However, there is a little focus on degradable plastics.

In 1968, J.R. Nixon et al. [23] studied the role of pH in the coacervation of the system; gelatin-water-ethanol and gelatin-water-sodium sulphate. Phase boundary determination, coacervate volume measurements, and analysis of the phase have been made to assess the influence of pH on the coacervation of gelatin solutions by ethanol and sodium sulphate. Coacervation was found to be pH independent. In the ethanol system

coacervation was noticeable only within a pH range in the vicinity of the isoionic point. In the sodium sulphate system, coacervation occurred at all pH values examined.

In 1995, G Weib et al. [24] studied the temperature and pH dependency of simple coacervate formation of hydroxypropyl methyl cellulose phthalate (HPMCP). Phase diagrams, quantitative investigations of the isolated polymer-rich phases and charge density measurements served to characterize phase separation. They found that coacervation formation of HPMCP is both temperature and pH-dependent. With increasing temperature the polymer content in the polymer-rich phase rose up to 23.6 %wt at 60°C corresponding to a polymer yield of 63.7%. Moreover, a minimum pH value of the HPMCP solution was required for coacervate formation.

In the same year, G Weib et al. [12] studied the microencapsulation of ibuprofen with HPMCP through simple coacervation. The microencapsulation process was controlled by temperature increase. SEM micrographs were used to demonstrate the microcapsule. They found that simple coacervation of HPMCP is a suitable method for the microencapsulation of ibuprofen. The results of SEM showed the high shell quality of microcapsules. The gelation of the polymer coats formed and the further processing of the microcapsules are performed at the increased temperatures (50°C).

In 1996, Byung Seon Yoon et al. [13] investigated degree of photodegradation and photodegradation after biodegradation of three degradable polymer materials; starch-polyethylene (PE) binary blends, PE containing starch and a photoactivator, and PE containing starch and photoactivator which was coated with biopolymer. Ferric dithiocarbamate and gelatin were selected as the photoactivator and coating material, respectively. The result showed that the addition of gelatin coated ferric salt in PE extended the induction period of degradation and accelerated photodegradation after removal of coating material by biodegradation.

2.6.4.1.1 Gelatin

Gelatin is a valuable raw material for microencapsulation by coacervation. It is nontoxic, inexpensive, and commercially available as well as has good film-forming property [26]. Gelatin molecules like those of other proteins that are large and complex. Values for the average molecule weight range from 15,000 – 250,000. Gelatin is composed of about 18 different amino acids which are linked together in an ordered fashion. Amino acids obtained by gelatin are shown in Table 2.7. Gelatin is composed of 50.5% carbon, 6.8% hydrogen, 17% nitrogen, and 25.2% oxygen.

Table 2.7 Amino acids obtained by complete hydrolysis of gelatin

Amino acids	%by wt	Amino acids	%by wt
Alanine	11.0	Methionine	0.9
Arginine	8.8	Phenylalanine	2.2
Aspartic acid	6.7	Proline	16.4
Glutamic acid	11.4	Serine	4.2
Glycine	27.5	Threonine	2.2
Histidine	0.78	Tyrosine	0.3
Hydroxyproline	14.1	Cystine	2.6
Leucine and isoleucine	5.1		Trace
Lysine	4.5		

2.6.4.1.2 Wall-Hardening Agents

Since the gelatin molecule contains amino and carboxyl groups, it can be insolubilized by cross-linking agents [27]. Many different agents can be used to harden gelatin-containing walls of microcapsules formed by simple coacervation.

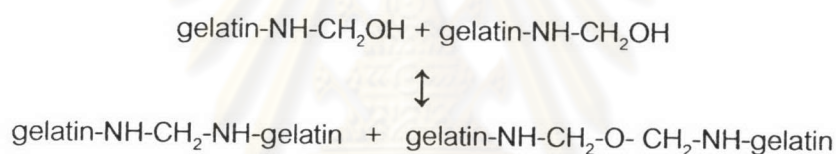
The most frequently used hardening agents for crosslinking gelatin-coated microcapsules are formaldehyde and glutaraldehyde.

The mechanisms of reaction with formaldehyde are followed by these steps [27].

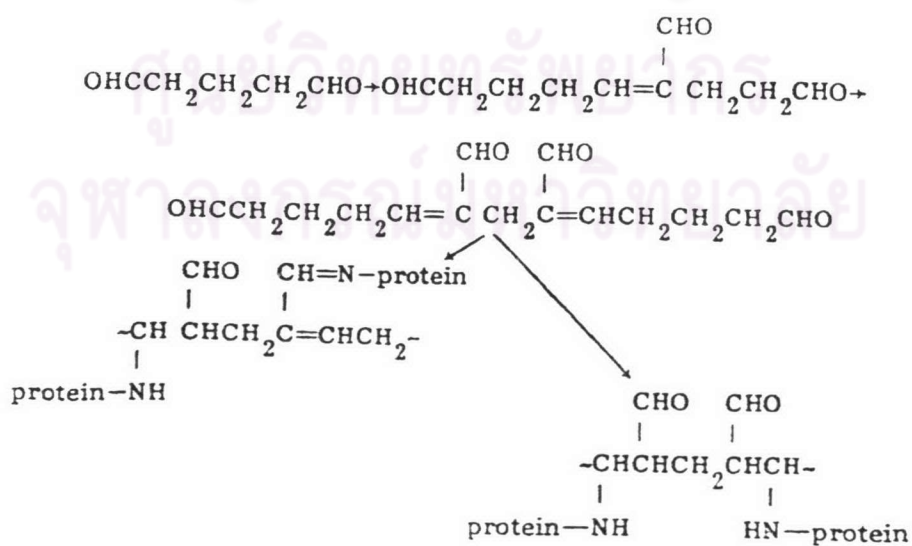
1. Formaldehyde reacts with amino groups of the gelatin as follow:



2. Two molecules of the product react to crosslink by means of a dimethylene ether bridge or a methylene bridge as follow:



Glutaraldehyde, largely polymeric and unsaturated aldehyde, reacts with proteins for hardening effect as follows [27].



There are a lot of researches working on the improvement of gelatin properties by crosslinking with hardening agent. For example;

In 1995, H. Akin and N. hasirci [14] studied the gelatin microspheres crosslinked with glutaraldehyde with different crosslink densities (4, 8, 16, 24 %wt). The microspheres were prepared by the phase separation technique induced by temperature change. Size and shape of the microspheres were examined with SEM and a narrow size distribution was observed. The glass transition temperature values increased with an increase in glutaraldehyde.

In 2000, P. G. Dalev et al. [21] investigated biodegradation of chemically modified gelatin films in soil by using different crosslinking agent (formaldehyde, glyoxal, glutaraldehyde, butadiene diepoxide, or diepoxyoctane). Their biodegradability were tested by soil burial testing in a laboratory environment under temperature and humidity control in 10 days. The relationship between weight loss and time of biodegradation showed a linear behavior for all the samples, but the rate of biodegradation showed a dependence on the type of crosslinking agent and the density of crosslinking.

In 2003, R.A. de Carvalho et al. [22] examined the modified gelatin based films with transglutaminase, glyoxal, and formaldehyde. The cohesion properties, barrier characteristics, the mechanical resistance, and decreasing the film solubility was investigated. They found that all properties were decreased when cross-linking with transglutaminase, glyoxal, and formaldehyde. The treated film showed a 7% decrease in solubility as compared to the untreated film.

2.6.4.2 Complex Coacervation

Complex coacervation involves the use of more than one colloid [8]. Gelatin and acacia in water are most frequently used. The coacervation is accomplished mainly by charge neutralization between the negative charge of acacia and the positive charge of gelatin at the pH below the isoelectric point of gelatin and the appropriate concentration condition. The deposition of coacervation droplets is aided by a reduction in total free interfacial energy of the system consequent upon the decrease in the surface area of coating material as its droplets coalesce around core material. The coating is then gelled by lowering the temperature and hardened by the addition of a crosslinking agent such as formaldehyde and glutaraldehyde. Finally, dried by the appropriate method, the desired microcapsules are collected.



ศูนย์วิทยทรัพยากร
จุฬาลงกรณ์มหาวิทยาลัย