CHAPTER I

INTRODUCTION

Polyaniline (PANI) is one of the most extensively studied conductive polymers. Potential applications include use in rechargeable batteries, sensors, switchable membrane, anticorrosive coatings, and electronic devices (Cho, 2004). Polyaniline is commercially attractive owing to its facile synthesis through either chemical or electrochemical methods, good environmental stability, ease of conductivity control, and inexpensive production in large quantity. However, like other conductive polymers, polyaniline by itself cannot be easily fabricated in the form of a thin film with good mechanical properties. Thus, its practical use has been limited.

A number of attempts have been made to fabricate polyaniline blends and composites with improved processibility and mechanical properties while retainning the inherent conductive properties of the polymer. Polyaniline blends can be prepared by blending polyaniline with other polymers in solution or melt state. Alternatively aniline can be polymerized chemically or electrochemically in the a solution of the matrix polymers. Polymers that have been used to prepare the conductive polyaniline blends include epoxy resin (Yang, 2003), polyethylene (Chipara, 2003), poly(vinyl alcohol) (Zhang, 2002; Mirmohseni, 2003; Gangopadhyay, 2001), polystyrene (Gupta, 2004), poly(acrylic acid) (Lima Pacheco, 2003), and poly(vinyl chloride) (Gupta, 2004). Recently, blends consisting of a conductive polymer and a hydrogel have attracted attention because they can form electroactive hydrogels that are capable of undergoing chemical and/or physical transitions in response to electrical potential. Therefore, the integration of these two types of materials has been investigated for the applications in biosensors (Brahim, 2002), and controlled drug release (Small, 1997). Examples of conductive polymer/hydrogel blends are polypyrrole/polyacrylamide (Small, 1997), polypyrrole/polyacrylic acid (Kim, 2000), and polypyrrole/poly(2-hydroxyethyl metharylate) (Brahim, 2002),

Chitosan, a copolymer of $\beta[1\rightarrow4]$–linked 2-acetamido-2-deoxy-D-glucopyranose and 2-amino-2-deoxy-D-glucopyranose, is generally obtained by deacetylation of chitin, which is the main component of the exoskeleton of crustacean

shells, such as shrimps. This polymer possesses hydrogel-like properties through reaction with glutaraldehyde as a crosslinking agent. In the form of a hydrogel, chitosan is widely used in pharmaceutical applications such as wound healing (Lloyd, 1998; Berger, 2004) and a drug delivery system (Puttipipatkhachorn, 2001; Nunthanid, 2004). The use of chitosan in the application of drug delivery system has attracted special interests. As a biocompatible, non-toxic, and hydrogel-like material, the chitosan is a medically suitable candidate as a drug carrier for various drug types. It has been shown (Puttipipatkhachorn et al., 2001; Nunthanid, 2004) that the drug release behavior of chitosan is mainly governed by the swelling property, the dissolution characteristic of the polymer films, the pK_a of the drug, and the drug-polymer interaction.

In the present work, polyaniline/chitosan blend films were prepared and mechanical and electrical properties were investigated in terms of blend composition and the condition of doping process: acid type, acid concentration, and doping time. Furthermore, the electrically stimulated controlled release behavior of the drug model from the blend film was investigated.

1.1 Theoretical Background

1.1.1 Conductive polymer

An organic polymer that possesses the electrical, electronic, magnetic, optical properties, and meanwhile retaining the mechanical properties, processibility of the conventional polymer is termed an 'intrinsically conducting polymer' (ICP), more commonly known as a 'synthetic metal'. For the past 50 years, conventional insulating polymer system have been increasingly used as substitutes for structural materials such as wood, ceramic, and metals because of their light weight, high strength, ease of chemical modification/customization, and processibility at low temperature. In 1977, the first electrically conducting organic polymer, doped polyacetylene, was reported, spurring interest in 'conducting polymer'. The common electronic feature of pristine (undoped) conducting polymeris a π-conjugated system which is form by the overlap of carbon p_z orbital and alternating carbon-carbon bond lengths shown in schematically in Figure 1.1. Other conducting polymers found are,

for examples, poly(p-phenylene) (PPP), polypyrrole (PPy), poly(p-phenylene)sulphide (PPS), polythiophene (PTh), polycarbazole (PCB), polyquinoline, and polyaniline(PANI)
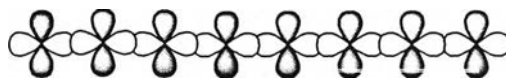

Figure 1.1 The π-conjugated system in the polyacetylene.

1.1.2 Conduction Mechanisms

Electrical conductivity is as function of the number of charge carriers of species 'i' (n_i), the charge on each carrier (ε_i), and carrier mobilities (μ_i). Conduction in solids is usually explained in the terms of the band theory which is described by the relation $\sigma = \sum \mu_i n_i \, \varepsilon_i$ where the unit of conductivity is S cm^{-1}. It is postulated that when atoms or molecules are formed in the solid state, the outer atomic orbitals containing the valence electrons are split into bonding and antibonding orbitals, and are mixed to form two series of closely-space energy level. These are usually called the valence band and conduction band, respectively. If the valence band is only partly filled by available electrons, or if the two bands overlab so that no energy gab exists between them , then the application of an electrical potential will raise some of electrons into empty levels where they will be free to move throughout the solid thereby producing a current. This is the description of a *conductor*. If, on the other hand, the valence band is full and is separated from the empty conduction band by an energy gap, then there can be no net flow of the electrons under the influence of an external field unless the electron are elevated into the empty band and this process will require a considerable expenditure of energy. Such materials are either semiconductors or insulators, depending on how large energy gap may be. The band model then assumes that the electrons are delocalized and can extend over the lattice. The majority of polymers are insulator.

For the electrical conduction in a polymer, the band theory is not totally suitable because the atoms are covalently bonds to another one, forming polymeric chains that experience weak intermolecular interactions. Thus macroscopic

conduction will require electron movements, not only along chains but also from one chain to another.

1.1.3 The Concept of Doping

Doping process describe as the method for achieving the high electrical conductivity. The doping of all conductive polymers is accomplished by the redox doping. This involves the partially addition (reduction) or removal (oxidation) of electrons to or from the π-system of the polymer backbone.

The concept of doping is of a unique underlying theme which distinguishes conductive polymers from all other types of polymers. During the doping process, an organic polymer, either an insulator or semiconductor, having a small conductivity, typically in the range 10^{-10} to 10^{-5} S cm^{-1}, is converted to the polymer which residues in the 'metallic' conducting regime (ca. 1 to 10^{4} S cm^{-1}). The controlled addition of known, usually small (< 10%) and non-stoichiometric quantities of chemical species results in dramatic change in electronic, electrical, magnetic, optical, and structural properties of the polymer. Doping can be reversible to produce the original polymer with a little or no degradation of the polymer backbone. Doping and undoping processes, involving dopant counterions which stabilize the doped state may be carried out chemically or electrochemically.

In the 'dope state', the polymer backbone of conductive polymer consist of a delocalized π-system. In the 'undoped state', the polymer may have a conjugated backbone such as in trans-$(CH)_x$ or it may have a non-conjugated backbone, as in polyaniline (leucoemeradine base form), which becomes conjugated only after doping or a non-conjugated structure as in the emeraldine base form of polyaniline which becomes conjugated only after protonic acid doping.
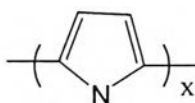
1.1.4 Doping Process

Doping process can be divided into three main types:

1.1.4.1 Redox Doping involving Dopant Ions
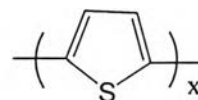
All conductive polymer (and most of their derivatives), e.g.
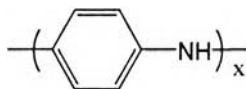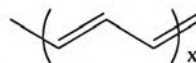

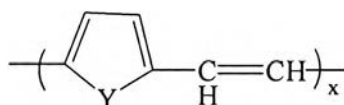Poly(p-phenylene)   Polypyrrole   Polythiophene

| Polyfuran | Polyaniline | Polyacetylene |

Poly(heteroaromatic vinylenes)

(where Y = NH, NR, S, and O); etc, undergo either p- and/or n-redox doping by chemical and/or electrochemical processes during which the number of electrons associated with the polymer backbone changes.

### 1.1.4.1.1 Chemical and Electrochemical p-Doping

p-doping, partial oxidation of the π-system of an organic polymer, was first discovered by treating *trans*-polyacetylene with an oxidizing agent such as iodine viz.

$$trans\text{-}[CH]_x + 1.5\, xy\, I_2 \longrightarrow [CH^{+y}(I^3)^-_y]_x \qquad (y < 0.07)$$

This process was accompanied by increase in conductivity from ca. 10^{-5} to 10^3 S cm^{-1}.

1.1.4. 1.2 Chemical and electrochemical n-doping

n-doping, partially reduction of the π-system of an organic polymer, was also discovered by using *trans*-polyacetylene and treating it with an reducing agent such as liquid sodium amalgam or preferable sodium naphthalide, viz.

$$trans\text{-}[CH]_x + (xy)Na^+ (Naphth)^- \longrightarrow [Na_y^+ CH^{-y}]_x + Naphth \qquad (y < 0.1)$$
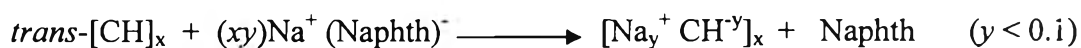
the antibonding π^* system is partially populated by this process which is accompanied by an increase in conductivity of ca. 10^3 S cm^{-1}.

### 1.1.4.2 Redox Doping involving No Dopant Ions

1.1.4.2.1 Photo-doping

When *trans*-polyacetylene, for example, is exposed to a radiation of energy greater than its band gap electrons are protonated across the gap and the polymer undergoes 'photo-doping'.

1.1.4.2.2 Charge–injection doping

It is the most conveniently carried out using a metal/insulator/semiconductor (MIS) configuration involving a metal and a conductive polymer separated by a thin layer of a high dielectric strength insulator. Application of an approxpriate potential across the structure can give rise, for example, to a surface charge layer, the 'accumulation' layer which has been extensively investigated for conductive polymer. The resulting charges in the polymer, e.g. $(CH)_x$ or poly (3-hexylthinylene) are present without any associated dopant ions so that the spectroscopic properties of the charged species so formed can be examined in the absence of dopant ions. However, the coulombic interaction between charges on the chain and dopant ions is a very strong interaction and one that can totally alter the energetic of the system. Studies of this type of polymers strongly suggest that the formation and role of bipolarons in the chemically and/or electrochemically doped polymers should be carefully re-examined since they may be stable only in the presence of the dopant counterion.

1.1.4.3 Non-redox doping

This type of doping process differs from the redox doping descried above in that the number of electrons associated with the polymer backbone does not change during the doping process. It is accomplished by treating an emeraldine base with aqueous protonic acids and it accomplished by nine to ten order of magnitude increase in conductivity (up to ca. 10^2 S cm^{-1}) to produce the protonated emeraldine base, viz.

2x HCl
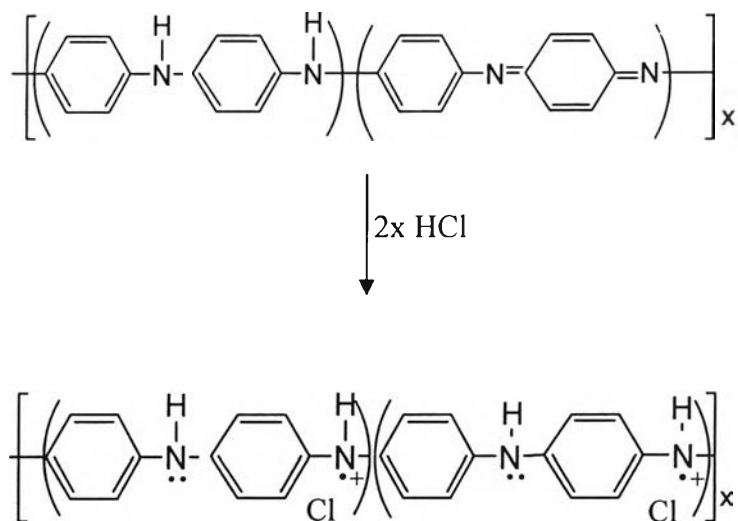
**Scheme 1.1** Doping process of emeraldine base by protonic acids.

1.1.5 Polyaniline

Polyaniline is one of the conductive polymers synthesized by chemical oxidation or by electrochemically polymerization in the presence of acid media. Polyaniline has a general formula containing reduced repeat units, and oxidized repeat units. The general formula of polyaniline is shown in the Scheme 1.2.

reduced repeat units   oxidized repeat units
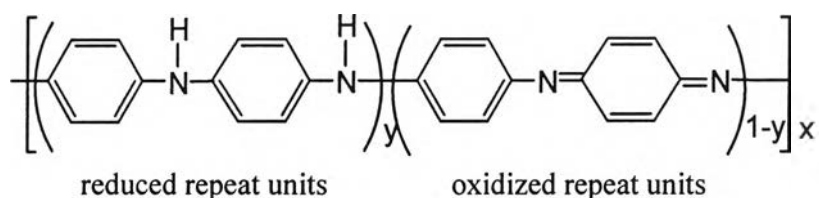
Scheme 1.2 The general formula of polyaniline.

Polyaniline can exist in three different oxidation states with different colours. The fully reduced form of polyaniline, Leucoemeraldine, corresponds to a value of y = 1; the fully oxidized form of polyaniline, Pernigraniline, corresponds to a value of y = 0; and the half oxidation form of polyaniline, Emeraldine, corresponds to a value of y = 0.5. The different oxidation states of polyaniline are shown in the Scheme 1.3.
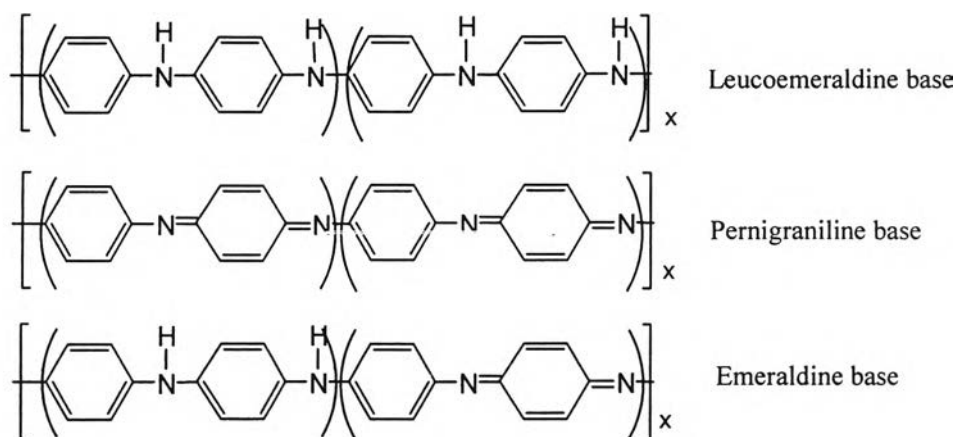
Scheme 1.3 The different oxidation states of polyaniline.

Each oxidation state can exist in the form of its base or its protonated form (salt) by treatment with an acid. The different oxidation states of polyaniline can interconverse process of polyaniline is shown in Scheme 1.4.

Pernigraniline base

Emeraldine base

Emeraldine salt

reduction ↑↓ oxidation

Leucoemeraldine base

Leucoemeraldine salt
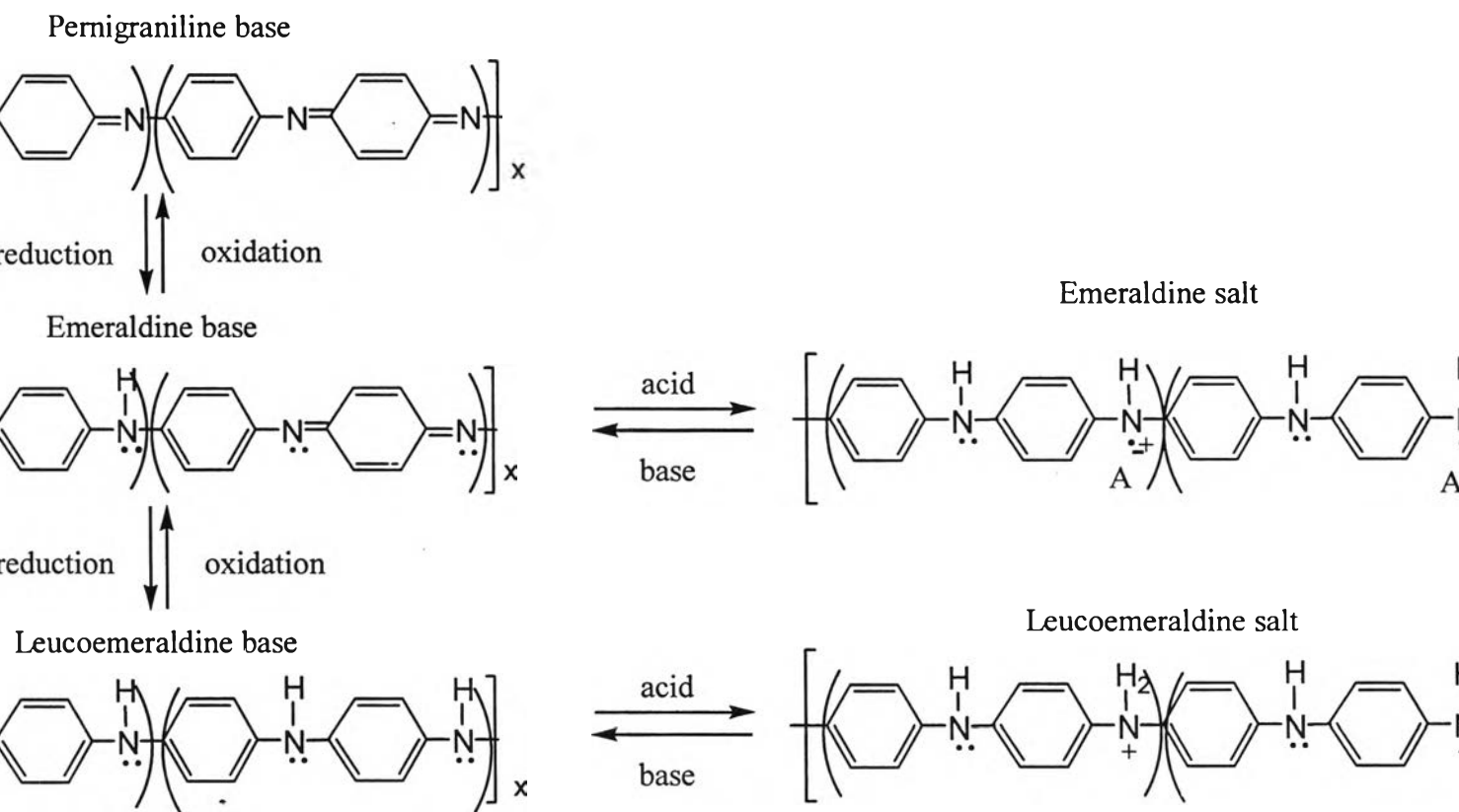
reaction diagram consistent with the interconversion of different oxidation and protonation states of polyaniline.

The insulating emeraldine base form of polyaniline can be converted to the conducting emeraldine salt form by two independent doping methods:

1) Oxidation doping method by chemical reaction with an appropriate oxidizing agent such as $FeCl_3$ and electrochemical charge transfer reaction. The charge transfer reaction causes a change in the total number of π-electron on the conjugate chain.

2) Protonation doping with acid-base reaction in the aqueous media with pH less than 2-3. There is no change in the number of π-electron.

In the recent years, polyaniline (PANI) has been considered as one of the most potential conducting polymers for various electrochemical, electrorheological and electronic applications such as batteries, sensors, controlling systems and organic displays because of its facile synthetic process, good environmental stability, easy conductivity control and cheap production in large quantities. However, its processability to make either films or coated layers is rather difficult because it is infusible and insoluble in common solvents and the product from pure polyaniline shows low mechanical properties, therefore, the above-mentioned commercial applications have been limited.

The general method used to solve these problems is to fabricate the polymer composite or polymer blend with other polymer matrix. The polymer composite of conductive polymer and other polymer matrix can enhance the processability and mechanical properties of the conductive polymer while the inherent properties of conductive polymer are still retained

1.1.6 Hydrogel

Hydrogel is a three-dimensional of hydrophlilic polymers in which a large amount of water is present. In general, the amount of water is at least 20% of the total weight. If water is composed of more than 95% of the total weight, then the hydrogel is called superabsorbant. The most characteristic properties of hydrogel are that it swells in the presence of water and shrink in the absence of water. The extent of swelling is determined by the nature (mainly hydrophilicity) of polymer chains and the crosslinking density. If hydrogel is dried, the swollen network of the hydrogel is collapsed during drying due to the high surface tension of water, and then it is called xerogel. Thus, the dried hydrogel become much smaller in size than the hydrogel

swollen in water. During swelling and shrinking process, hydrogel can preserve its overall shape.

To maintain the three-dimensional structure, polymer chains of hydrogels are usually crosslinked either chemically or physically. In chemical gels polymer chains are connected by covalent bonds. And thus it is difficult to change the shape of chemical gels. On the other hand, polymer chains of physical gels are connected through non-covalent bonds, such as van der Waals interaction, ionic interaction, hydrogel bonding, or hydrophobic interaction. Since the bondings between polymer chains are reversible, physical gels possess sol-gel reversibility. For example, sodium alginate becomes a gel in the presence of calcium ions, but the gel becomes sol if the divalent cations are removed.

Hydrogels are currently being studied as controlled release carrier of drug and proteins because of their good tissue compatibility, easy manipulation under swelling condition and solute permeability. There are two general methods for loading the drug models into hydrogels as drug carrier. In one method, a hydrogel monomer is mixed with drug initiator and crosslinking agent and is polymerized to entrap the drug within the matrix. In another method, a performed hydrogel (in most case lyophilized) is allowed to swell to equilibrium in a suitable drug solution. The release of these drugs from the hydrogel delivery system involves absorption of water into the polymer matrix and subsequent diffusion of the drug as determined by Fick's law. Kim *et al.* reviewed the detailed consideration of swelling, drug loading, and drug release. They reported that factors that affect the drug release from hydrogels include the drug loading method, the local partition of drugs, the overall hydrophilic/hydrophobic balance, the osmotic effect of dissolved drug, and the polymer chain elasticity. The preparation of hydrogel matrix for a specific drug carrier should be tailored considering the aforementioned effects as well as the physical properties of drugs, loading level, and release kinetics.

The example of hydrogel available today are include poly(2-hydroxylethyl methacrylate) (pHEMA), poly(ethylene oxide) (PEO), poly(vinyl alcohol) (PVA), which are the synthetic hydrogel. While, the nature occurring hydrogel are include alginate, chitin, chitosan and their derivative.

1.1.7 Chitin and Chitosan

1.1.7.1 Source of Chitin and Chitosan

Chitin occurs in a wide variety of species, from fungi to the lower animals. Arthropod shells (exoskeletons) are the most easily accessible sources of chitin. These shells contain 20-50% chitin on dry weight basis. From a practical viewpoint, shells of crustaceans such as crabs and shrimps are conveniently available as wastes from· seafood processing industries and are used for the commercial production of chitin. Other potential sources of chitin production include krill, crayfish, insects, clams, oysters, jellyfish, algae, and fungi. Krill is likely to be the most promising source in the future.

Squid pens also contain chitin that is classified as β-chitin. This material is distinguished from the ordinal α-chitin in the crustacean shells according to the difference in the crystalline structure. β-chitin has weaker intermolecular forces and is quite attractive as another form of chitin having some characteristics considerably different from those of α-chitin. The chemistry of β-chitin is rapidly advancing, although this starting material is less abundant and is not yet produced commercially. The cell walls of some fungi (Zygomycetes) contain chitosan as well as chitin and these may be used as sources of chitosan. Practically, however, chitosan is more easily prepared by the deacetylation of chitin.
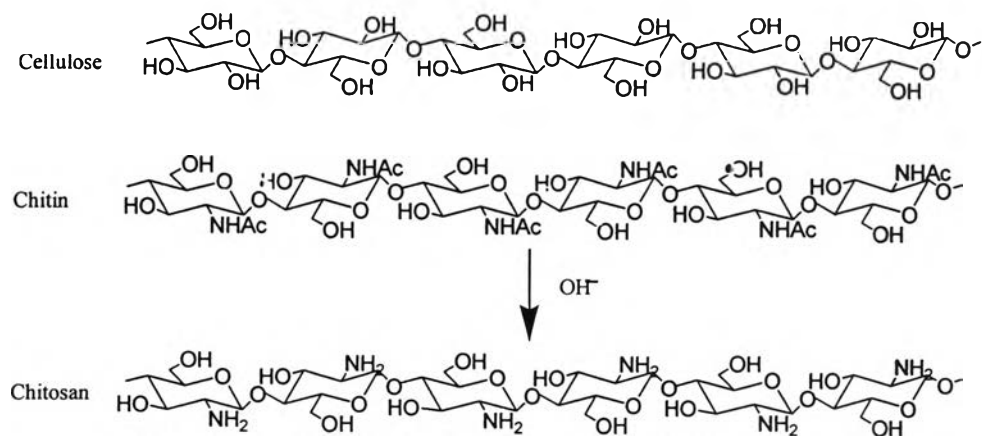
Scheme 1.5 Structure of cellulose, chitin, and chitosan.
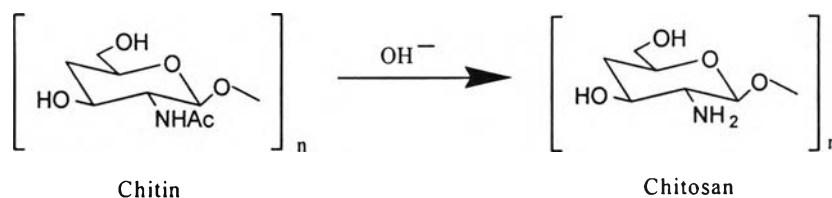
1.1.7.2 Preparation of Chitin

α-chitin is produced commercially from crab and shrimp shells, which contain calcium carbonate and protein as the two other major components. Pigments are also contained in small quantities. Furthermore, the chitin molecules are assumed to have polypeptide side chains attached covalently to some of the C-2 amino groups through amide linkages. Chitin is the most stable substance against acid and alkali among these components and not is soluble in ordinary solvents. Accordingly, it can be isolated as a residue, which remains after decomposing the other substances present in the shell with acid and alkali.

The shells are first cleaned and treated with diluted hydrochloric acid at room temperature to remove calcium carbonate. The decalcified shells are then cut into small flakes or are pulverized and heated in 1-2 mol/l sodium hydroxides near 100°C to decompose the proteins and pigments. Chitin is obtained as almost colorless to off-white powdery material. There are some free amino groups besides acetamide groups, and the degree of deacetylation for the isolated chitin is around 0.1. Proteases may be used to remove some of the proteins under mild conditions.

β-chitin can be isolated from squid pens in a similar but simpler manner, since squid pens are composed almost exclusively of chitin and proteins with only trace amount of metal salts. Moreover, the molecular packing of β-chitin is less tight. Squid pens can be treated with hydrochloric acid and sodium hydroxide under mild condition to give β-chitin. When the isolated chitin is pulverized within an ultra-centrifugal mill, a white fluffy cotton-like material is obtained. During the isolation procedure, some of the acetyl groups are removed, and the resulting chitin has a degree of deacetylation near 0.1.

1.1.7.3 Preparation of Chitosan

Chitosan itself occurs in some fungi and can be isolated from their cell wall. It is formed by the action of the chitin deacetylase on the precursor chitin. Further detailed studies, however are necessary for the practical production of chitosan, although the feasibility of its preparation has been demonstrated.

Scheme 1.6 Deacetylation of chitin.

Chitosan is commonly prepared by deacetylating α-chitin using 40-50% aqueous alkali at 100-160°C for a few hours (Scheme 2). The resulting chitosan has a degree of deacetylation up to 0.95. For complete deacetylation, the alkaline treatment can be repeated. Chitosans with various extents of deacetylation and grades are now commercially available. The deacetylation of β-chitin isolated from squid pens proceeds much more rapidly under similar conditions, but this results in the formation of heavily colored chitosan. Since β-chitin can be deacetylated at a much lower temperature than α-chitin, a reaction near 80°C is adequate for deacetylation as well as for the suppression of coloration processes, giving almost colorless chitosan products.

1.1.8 Electrically Stimulated Controlled Release System

Transmembrane solute flux can be modulated by the action of an electric field on the membrane and/or directly on the solute. The electrophoretic migration of a charged macrosolute within a hydrated membrane results from the combined response to the electrical forces on the solute and its associated counterions in the adjacent electrolyte solution. Grimshaw *et al.* have recently demonstrate four distinct electrochemical and electromechanical mechanisms for selective controlled transport of protein and neutral solutes across hydrogel membranes: (1) electrochemically and chemically induced swelling of the membrane to alter the effective pore size and permeability; (2) electrophoretic augmentation of solute flux within the membrane; (3) electroosmotic augmentation of solute flux within the membrane; (4) electrostatic partitioning of charged solute into the charged membranes.

Pasechink et al. reported an increase in the effective pore radius of ultrafiltration membranesdue to the electrodinamic effects. Burmeyer and Murray observed changes in the ionic permeability of polypyrrole redox membranes using the

voltage-controlled electrochemical reaction. Bhaskar et al. affected the permeability of liquid crystalline membranes to small organic solute, applying transmembrane electric fields, which caused a phase change by alignment of the polymeric molecules. Electric fields can cause changes in the membrane ionization states, affecting membrane hydration and permeability. Eisenberg and Grodzinsky alter the restricted diffusion of sucrose through the collagen membranes via electrodiffusion (effect of the electric field on concentration profiles within the membrane), producing flux changes up to 25%. Nussbaum and Grodzinsky demonstrated reversible changes in the uniaxial swelling of PMMA membranes via electrodiffusion control of intramembrane ionic strength. Weiss et al. produced a 16-fold increase in the permeability of similar PMMA membranes to 10 kDa dextran by using the electrolysis reaction at a platinum cathode to alter bash pH and, hence, membrane hydration. Osada induce the release of pilocarpine into the surrounding solution when a DC electric field of 6 V/cm was applied to PMMA gels incorporated with pilocarpine.

Application of an electric field across a hydrated polyelectrolyte membrane, such as PMMA, gives rise to a net force on the space charge in the fluid phase, which contains an excess of counterions over coions; this force is transferred to the solvent, resulting in the electrosmotic fluid flow relative to the solid membrane matrix.

Electrosmotic transport of water therefore can enhance or oppose the diffusive transport of a neutral or charge solute. With charged membranes and charged solute, an application of an electric field can result in control of solute flux by the combination of electrophoretic and electrosmotic mechanisms.

D'Emanuele and Stainforth et al. proposed a drug delivery divide which consists of a polymer reservoirwith a pair electrodes placed across the rate limiting membrane. By altering the magnitude of the electric field between the electrodes the authors proposed to modulate the drug release rates in a controlled and predictable manner. A linear relationship was found between current and propanolon HCl permeability through poly(2-hydroxyethylmethacrylate) (PHEMA) membranes crosslinked with ethylene glycol (1% v/v). Buffer ionic strength as well as electrode polarity was found to have significant effect on the drug permeability.

A different approach to electrochemically controlled release is base on polymer which binds and release bioactive compounds in response to an electric signal. The polymer has two redox states, only one of which is suitable for ion binding. Drug ions are bound in one redox state and release from the other. The attached electrodes serve to switch the redox states and the amount of current passed can control the amount of ions released.

The mechanisms described for electrically controlled membrane permeability are of current interest in the field of electrically controlled or enhanced transdermal drug delivery (e.g. iontophoresis).

The current/voltage for electrically stimulated controlled release application shouls: (1) be sufficiently high to provide a desired delivery rate; (2) not produce anyharmful effects on the skin including a permanent alteration on the skin permeability; (3) establish a quantitative relationship between the flux and applied current/voltage; and (4) maintain constancy of the current/voltage during the experimental period. In addition, the drug should be electrochemically stable.

Recently, in order to overcome charge build up, irritation and burning of skin in the area of prolonged continuous current electrode application, a pulse current approach was evaluated. In this approach the current was turned on and off in short intervals. Using the pulse current iontophoresis the skin can tolerate much higher voltage and current conditions.