CHAPTER II

REVIEW OF RELATED LITERATURE AND RESEARCH

This thesis focused on the preparation of chitosan/carboxymethylchitosan (CMC) hydrogels modified with polydimethylsiloxane (PDMS) or poly(ethylene glycol) (PEG). This chapter thus provides the information and background regarding chitosan, carboxymethylchitosan (CMC), polydimethylsiloxane (PDMS), poly(ethylene glycol) (PEG), and semi-Interpenetrating Polymer Network (semi-IPN), respectively.

Introduction to chitin-chitosan

Chitin, the second most abundant biopolymer on earth [25], can be naturally found in crab shell, shrimp shell and squid pen and chitosan is the partially deacetylated form of chitin. Chitin-Chitosan is recommended as suitable function materials because it possesses excellent properties such as biocompatibility, biodegradable, non-toxicity, and adsorption ability [26]. They are presently available for uses in biomedical, medicine, pharmaceuticals, food and agricultural applications. For instance, they are capable to adsorb metal-ions (Cu^{2+}, Hg^{2+} and Ni^{2+}) from waste water or to remove color from textile. In the cosmetic point of view, they are used as permanent waving lotions. In medical aspect, they are used as artificial skin.

In general, Thailand is capable to produce and import approximately 390,000, 57,000 and 190,000 tons/year of shrimp, crab and squid, respectively. In particular, biowaste from shrimp, such as head, shell and tail, is more than 10,000 tons/year [27]. Chitin production capability of the companies in Thailand is in the range of 3-240 tons/year, 80% of which is exported, while those of chitosan is in the range of 2.4-12 tons/year; most of them is for local consumption and about 20% of them is exported [27].

1. Chitin

Chitin $(C_5H_{13}NO_5)_n$ or poly (1, 4-β-2-acetamido-2-deoxy-D-glucose) (Figure 1), has the elemental composition of 47.29% carbon, 6.45% hydrogen and 39.37% oxygen [28]. It is dissolvable only in acidic aqueous solutions such as hydrochloric acid, sulfuric acid, acetic acid and phosphoric acid. It is however insoluble in most common organic solvents.

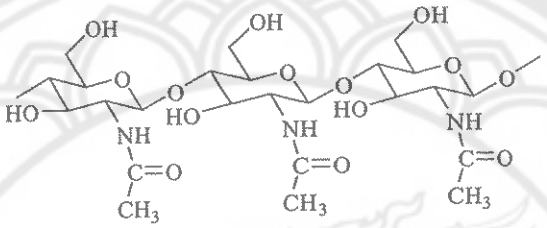


Figure 1 Structure of chitin

Chitin predominantly presents as a fibrillar crystalline material [29]. Based on infrared spectroscopy and x-ray diffraction data, chitin can be found in one of the three crystalline forms: α-Chitin, β-Chitin and γ-Chitin.

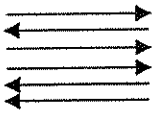
- α-Chitin form

α-Chitin is arranged very tightly in an anti-parallel fashion. α-Chitin mainly presents in shell of crabs, lobsters and shrimps.

- β-Chitin form

β-Chitin is arranged in a parallel fashion. It mainly exists in squid pens.

- γ-chitin form



γ-Chitin is the form in which the molecules are arranged in both parallel and anti-parallel manners. γ-Chitin is primarily found in fungi and unicellular plant.

As a result of the molecular packing, intermolecular interactions in β-chitin are weaker than those in α-Chitin, making β-Chitin being more susceptible to dissolution in a number of solvents, more reactive toward chemical reactions and versatile in uses.

2. Chitosan

Chitosan is composes of 2-amino-2-deoxy-β-D-glucopyranose (D-glucosamine) and N-acetyl-D-glucosamine residues (Figure 2). Chitosan is a derivative of chitin which is obtained by deacetylation reaction to remove acetyl groups from *N*-acetly glucosamine sugar. Chemical structure of chitin and chitosan rather resemble to that of cellulose [30].

The molecular weight of chitosan, for commercial product, varies within the range of 10,000-1,000,000 g/mol depending on processing conditions. Mole fraction of deacetylated units (glucosamine units), defining as the degree of deacetylation, usually ranges from 70-90% [31].

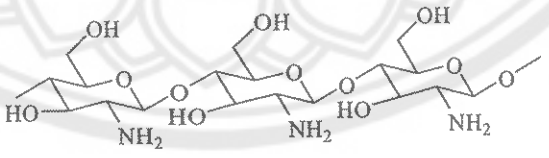


Figure 2 Structure of chitosan

Chitosan is semi-crystalline natural polymer where its degree of crystallinity is dependent on the degree of deacetylation [29]. The degree of deacetylation is one of the most important chemical characteristics of chitosan. It is also used to determine the free amino content in structure. Chitosan is insoluble at

neutral and alkaline pH but it is soluble in organic acids such as hydrochloric acid, lactic acid and acetic acid. In acidic medium, the amine groups of the polymer are protonated, resulting in a soluble, positively charged polysaccharide that has a high charge density. Chitosan is a natural, nontoxic, biodegradable polysaccharide and commercially available in the forms of solution, flake, fine powder, bead and fiber.

3. Physical and chemical properties of chitosan

3.1 Solubility [32]

Chitosan is a cationic polymer having a pKa of about 6.3. It is thus soluble in acidic aqueous solutions. Its solubility is dependent on the presence of free amino groups capable of being protonated when it is dissolved in acidic aqueous solutions.

3.2 Degree of deacetylation

Chitosan is considered as a copolymers containing two different monomer units, anhydro-N-acetyl-D-glucosamine and anhydro-D-glucosanmine. The degree deacetylation of chitosan can be measured by many methods such as infrared spectroscopy, titration, gas chromatography [33], gel permeation chromatography [34] and dye adsorption. The molecular weight, structure and properties of chitosan are affected by the degree of deacetylation.

3.3 Viscosity

The apparent viscosity of chitosan solution is dependent on its molecular weight, its concentration and the temperature of the solution. The viscosity increases with an increase in molecular weight and concentration of chitosan, while its viscosity decreases with an increase in temperature.

4. Applications of chitosan

Chitosan possesses a variety of intriguing properties such as biocompatibility, biodegradability, non-toxic and absorption properties, so that it is used in various applications, such as biomedical material, medicine, cosmetic, pharmaceuticals and food [34].

A summary of potential applications of chitosan is shown in Table 1.

Table 1 Potential applications of chitosan [26]

Applications	Machanisms
Water engineering	- It shows a potential to remove metal-ions (Cu^{2+}, Hg^{2+} and Ni^{2+} etc.) from waste water. - Color removal from textile mill effluents. Due to its unique molecular structure, chitosan has an extremely high affinity for many classes of dyes.
Paper finishing	- Chitosan has been reported to impart wet strength to paper. Hydroxymethyl chitin and other water-soluble derivatives are useful additives in paper making. The entrepreneur in paper making untilizes this polymer for better finish paper properties.
Solid-state batteries	- Chitosan is a biopolymer which provides ionic conductivity when dissolved in acetic acid solutions. Its conductivity is attributed to the presence of protons from the acetic acid solutions. The transport of these protons is thought to occur through microvoids presented in the polymer.
Photography	- Chitosan has important applications in photography due to its resistance to abrasion, its opical characteristics, and film forming ability.
Drug-delivery system	- Chitosan is non-toxic and easily bioabsorbable with gel-forming ability at low pH. Moreover, chitosan can prevent or weaken drug irritation in stomach. Also, chitosan matrix formulations appear to float and gradually swell in an acid medium. All these interesting properties of chitosan make this natural polymer an ideal candidate for controlled drug release formulations.

Table 1 (cont.)

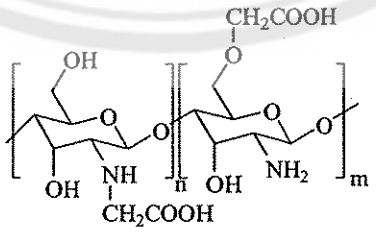
Applications	Machanisms
Drug-delivery system	- Chitosan is non-toxic and easily bioabsorbable with gel-forming ability at low pH. Moreover, chitosan can prevent or weaken drug irritation in stomach. Also, chitosan matrix formulations appear to float and gradualely swell in an acid medium. All these interesting properties of chitosan make this natural polymer an ideal candidate for controlled drug release formulations.
Fat trapper	- Chitosan attaches itself to fat in stomach before it is digested; thus chitosan traps fat and prevents its absorption by the digestive tract. Fat in turn binds to chitosan fibre, forming a mass such that the body can not absorb and it is then eliminated by body. Chitosan fibre differs from other fibres in that it possesses a positive ionic charge, which gives it the ability to chemically bond with the negatively charged lipids, fats and bile acids.
Cosmetics	- Chitosan has fungicidal and fungistatic properties. It is the only natural cationic gum and used as creams, lotions and permanent waving lotions.
Artificial skin	- Chitosan can be used as artificial skin. It is applicable to long-term chronic use as a nonantigenic membrane, which performs as a biodegradable template for synthesis of neodermal tissue. Chitosan has structural characteristics similar to that of glycosamino glycans, so it could be considered for further development for use as skin replacement.

Table 1 (cont.)

Applications	Machanisms
Food and nutrition	- Animal nutritional studies have shown that the utilization of diet food may be improved if it contains small amounts of chitinous material. This improvement is attributed to the change in the intestinal microflora brought about by the chitinous supplement.

5. **Carboxymethylchitosan (CMC)**

A limitation of chitosan for extensive applications is that it dissolves only in acidic aqueous solutions. Because amino groups in chitosan are weak bases, they are thus predominantly protonated when pH < 6.5, leading to the solubilization of the polymer only in dilute acidic solutions. This drawback renders them difficult to process or modified with other molecules. Grafting hydrophilic reagents or polymers onto chitosan were reported as a technique to improve its solubility in water or organic solvents. One of them was the carboxymethylation of chitosan through the direct alkylation using the monochloroacetic acid reagent. The reactive sites for the carboxymethylation of chitosan are the amino and hydroxyl groups being present in its chain. According to the literature, some carboxymethylated chitosan derivatives and their applications have been studied [18]. The choice of the appropriate reaction conditions and reagents allows the preparation of *N*-, *O*-, *N*, *O*- or *N*, *N*-dicarboxymethylchitosan (Figure 3).



N,*O*-carboxymethylchitosan (CMC)

Figure 3 Chemical structure of carboxymethlychitosan (CMC)

In 2006, Liping Sun *et al.* have reported the synthesis of quaternized carboxymethylchitosan (QCMC) from the reaction between CMC and *N*-quaternary ammonium group in the presence of 2,3-epoxypropyl trimethyl ammonium. They found that QCMC had a strong antimicrobial activity [17]. In the same year, Lichen Yin *et al.* prepared superporous hydrogels containing poly(acrylic acid-*co*-acrylamide)/*O*-carboxymethyl chitosan interpenetrating polymer networks (SPH-IPNs). SPH-IPNs were prepared by crosslinking *O*-carboxymethylchitosan (*O*-CMC) with glutaraldehyde (GA) and they showed an enhanced loading capacity of insulin with more than 90% of the insulin released within 1 h [19].

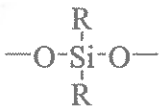
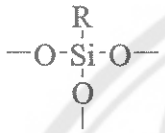
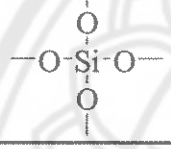
Polydimethylsiloxane (PDMS)

1. Introduction to polysiloxane

Silicone is a commercial name of polysiloxane. It is the most extensively studied class of semi-inorganic polymers over the last forty years. They are structurally comprised of silicon atoms bound to each other through oxygen atoms. Because of the combination of inorganic and organic character in their backbones, polysiloxanes provide a wide range of properties that are not found in other organic polymers [35]. Polysiloxane is a highly flexible biomaterial due to its low glass transition temperature (T_g = -125°C) [36]. It is thus used as an elastomeric modifier in various applications. Additionally, other unique properties of polysiloxane, e.g. low toxicity, good biocompatibility, high oxygen permeability, good thermal and oxidative stability, are also suitable for use as biomaterials [37].

Silicon atom in polysiloxanes can be covalently bound to one, two or three organic hydrocarbon substituents, resulting in trifunctional (T), difunctional (D) or monofunctional (M) siloxanes, respectively (Table 2). Polydimethylsiloxane or PDMS is the best known polysiloxane used in most applications. It also was classified as difunctional polysiloxane (D) with dimethyl groups (R=CH_3) in its repeating unit.

Table 2 Structural units of the polysiloxanes [35]

Structure formula	Composition	Functionality	Symbol
R_3Si-O-	$R_3SiO_{0.5}$	Monofunctional	M
	R_2SiO	Difunctional	D
	$RSiO_{1.5}$	Trifunctional	T
	SiO_2	Quadrifunctional	Q

Historically, in 1863, Friedel and Craft prepared tetraethyl silane by zinc diethyl reacted with silicon tetrachloride

$$2\ Zn(C_2H_5)_2 + SiCl_4 \longrightarrow 2\ ZnCl_2 + Si(C_2H_5)_4$$

In 1872, Ladenburg synthesized polysiloxane by the reaction of diethoxydiethyl silane with H_2O and acid. The resultant products were in the oil-like form with high viscosity.

$$C_2H_5-O-\underset{\underset{C_2H_5}{|}}{Si}-O-C_2H_5 \xrightarrow[\text{Acid}]{H_2O} C_2H_5OH + \left(O-\underset{\underset{C_2H_5}{|}}{Si}\right)_n$$

Polysiloxanes are high flexibility polymers due to their exceptionally low bond rotational energy barrier around Si-O bonds compared to hydrocarbon compounds (Table 3). This freedom of rotation imparts unique and intriguing properties, e.g. an extremely low glass transition temperature (-125 °C for PDMS), a large molar volume (75.5 cm^3/mole), low surface tension (20 mN/m for PDMS), and low viscosity. This is generally due to the long Si-O bond length combined with the open structure of the polysiloxane backbone.

Table 3 Silicon and carbon bond rotational energy barriers [35]

Bond	Energy (kJ/mole)
Si-O	< 0.8
C-O	11.3
$Si-CH_3$	6.7
$C-CH_3$	15.1

The Si-O skeleton bond has a length of 1.64 Å which is significantly longer than C-C single bonds (1.53 Å) in organic compounds. This leads to a reduction of steric interferences or intramolecular congestion. In PDMS, the bond angles of 143 degree in Si-O-Si and 110 degree in O-Si-O are significantly more than the tetrahedron bond angle of 109.5 degree in hydrocarbon chains, resulting in a more open structure and the low rotational energy barrier in polysiloxanes (Figure 4) [38].

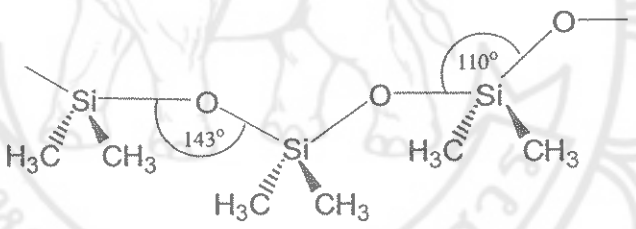


Figure 4 PDMS chains showing bond angles in the siloxane skeleton [38]

2. Preparation of polysiloxane

2.1 Preparation of cyclosiloxane [39].

Cyclosiloxane was prepared *via* various procedures. Since dichloro-dimethylsilanes are commercially available, hydrolysis of these reactive precursors is the most common method for preparing cyclosiloxanes. Dichlorodimethylsilane can be easily hydrolyzed to give an unstable diol which spontaneously undergoes condensation to produce mixtures of polydimethylsiloxanes (PDMS) and dimethylsiloxane cyclics (Figure 5) [39]. The cyclics, predominantly x=4-6, can be recovered by fractional distillation.

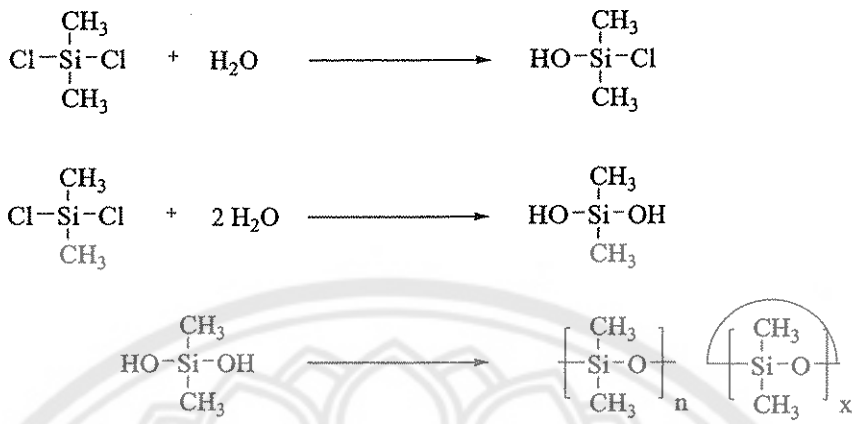


Figure 5 Hydrolysis of dicholodimethylsilane to produce polydimethylsiloxane (PDMS) and dimethylsiloxane cyclic [39]

The proportions of linear and cyclic siloxanes generated strongly depend on the reaction conditions. To obtain high yields of cyclosiloxanes, it is necessary to increase intramolecular condensation and simultaneously control the extent of intermolecular condensation in such a way that the degree of the condensation is about 4. Intramolecular condensation is facilitated over intermolecular condensation by low concentrations of the reactants. Thus, the slow addition of dimethyldichlorosilane to an excess of water favors the production of cyclics [35]. If a solvent is used in the reaction, a water-miscible solvent, e.g. methanol, also favors the production of the cyclics. The polarity of the solvent also has a significant effect on formation of cyclic compounds.

The thermodynamically stable cyclotetrasiloxane, D_4, is typically manufactured by the process discussed above. It is commonly used as a monomer for the equilibrium reaction to prepare PDMS because of its cost-effectiveness. The strained cyclotrisiloxane, D_3, is typically used as a monomer for living anionic polymerization. Hexamethylcyclotrisiloxane is commercially prepared using 1, 3-dihydroxy-1, 1, 3, 3-tetramethyldisiloxane and dichlorodimethylsilane in the presence of pyridine as a proton scavenger (Figure 6) [35]. Condensation of dichlorodimethylsilane in the presence of 10 mol% excess of zinc oxide also yields hexamethylcyclotrisiloxane [40]. Cyclotrisiloxanes with different substituents can be prepared by the same process using corresponding precursors.

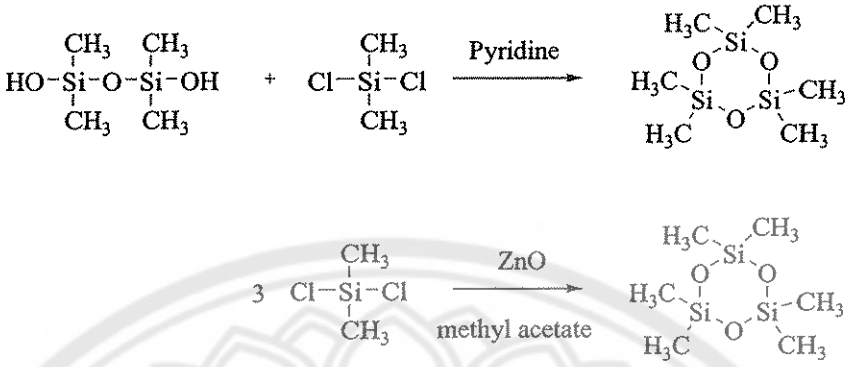
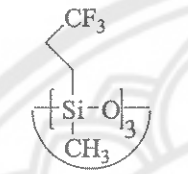
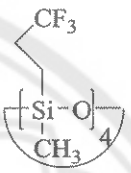
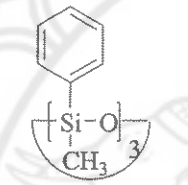
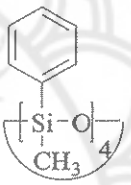
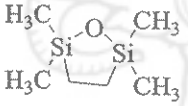
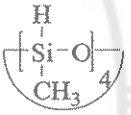


Figure 6 Preparation of hexamethylcyclotrisiloxane [35]

2.2 Equilibrium ring-opening polymerization of cyclosiloxanes: thermodynamic control

The general routes commercially used for preparing polysiloxanes are acid and base catalyzed equilibration polymerizations. Unstrained cyclics, e.g. D_4, are typically used as monomers for preparing polysiloxanes *via* this process. Utilization of a strained cyclic, e.g. tricyclosiloxane or D_3 (12-15 kJ/mole) has also been reported [41]. Other monomers which have been used in this process, including both strained and unstrained rings, are shown in Table 4. It is well known that siloxane bonds are exceptionally thermally stable. In the presence of strong acid or base, however, rearrangement or the so-called 'redistribution' or 'equilibration' of the siloxane bond takes place [42]. The siloxane bonds in both cyclic and linear species are continuously broken and reformed until the reaction reaches the thermodynamic equilibrium state. At equilibrium, a distribution of cyclics and linear polymers are obtained. The molecular weights of these linear polymers have a relatively broad. Gaussian distribution compared to the distributions produced via living anionic polymerization [43].

Table 4 Typical cyclosiloxane monomers used in the ring-opening polymerization [38]

Strained Rings	Unstrained Rings
D_3	D_4, D_5, D_6, D_7
	
	
	

A wide variety of catalysts has been used in this reaction, such as ion-exchange resin [44], UV radiation [45], Lewis acid, electron-deficient organosilicon reagents [46] and organic acid. Trifluoromethanesulfonic acid (triflic acid) [47] has been most widely used. Many mechanisms have been proposed but the acid-catalyzed equilibration mechanism is still not fully understood. It has been proposed that, in the presence of a protonic acid, e.g. sulfuric acid, oxygens in siloxanes are first protonated to form ≡Si-$^{+}$OH-Si≡ species. These protonated species are then attacked by nucleophiles at the partially positive silicon atoms and and eventually the Si-O bonds cleave (Figure 5) [35].

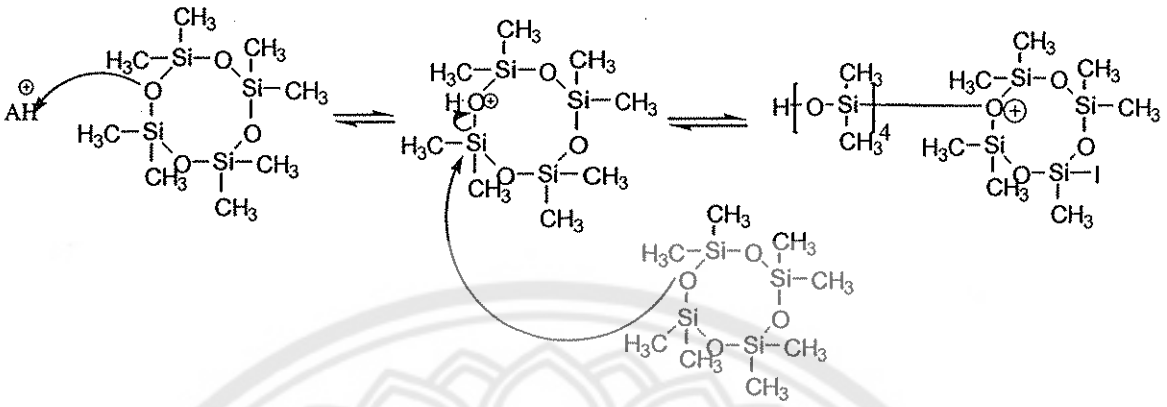


Figure 7 Proposed mechanism of acid-initiated ring-opening polymerization of D_4 [35]

3. Properties of polysiloxane [48]

3.1 Thermal stability

Thermal stability of polysiloxane stems from the thermal resistance of Si-O and Si-CH_3 bonds in polysiloxane structure. However, the partially ionic nature of these bonds (51%) means that they can be easily destroyed by concentrated acids and alkalis at ambient temperatures.

3.2 Mechanical properties

Polysiloxane has high tear and tensile strength, and high flexibility due to its extremely low glass transition temperature.

3.3 Electrical properties

Polysiloxane shows excellent electrical insulating properties with volume resistivities as low as 0.004 ohm.cm. This indicates that properties such as volume resistivity, dielectric strength and power factor are not affected as the temperature changes.

3.4 Biocompatibility

FDA (Food and Drug Administration) and ISO (International Strandards Organization) have verified that polysiloxane has no danger to human.

3.5 Chemical resistance

Polysiloxane well resists to water, chemicals, and oxidizing agents. However, it does not resist to high concentrations of acid and alkali solutions due to its molecular structure consists of 51% of ionic bonds (Si-O, Si-CH_3).

3.6 Gas permeability

Gas permeability of polysiloxane at 25°C is approximately 400 times greater than that of butyl rubber, enabling this material to be used in gas permeable applications such as oxygen permeable membranes in medical applications.

3.7 Resistance to hydrocarbon fluid, oils and solvents

The first compositions of polysiloxane that exhibit good oil resistance are those comprising of nitrile substituents (CN) in polysiloxane structure. They are superseded by polysiloxane containing fluorine, which displays excellent resistance to oils, hydrocarbon fluids and solvents.

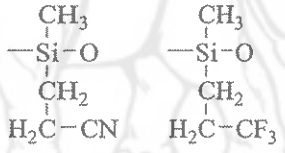


Figure 8 Oil resistant grades of polysiloxane with (left) nitrile functional groups and (right) fluorine functional groups [48]

4. **Applications of polysiloxane** [48]

There are four main industrial classes of polysiloxanes or silicone:

4.1 High Temperature Vulcanising (HTV)

It is sometimes called "heat curable rubbers". It is usually used in a semi-solid gum form in the uncured state. It requires rubber-type processing to produce finished items.

4.2 Room Temperature Vulcanising (RTV)

It usually comes as a flowable liquid used for sealants, mould making, encapsulation and potting. It is not generally used as conventional rubber.

4.3 Liquid Silicone Rubber (LSR)

It is sometimes called "heat curable liquid material". It can be processed on specially designed injection moulding and extrusion production equipment.

4.4 Silicone resin

It is prepared from oligosiloxane to obtain branch and cage like structure.

A summary of potential industrial applications of polysiloxane is shown in Table 5.

Table 5 Applications of silicone rubber [49]

Silicone resin	**RTV**
Adhesives	Adhesives
Encapsulants	Electric insulation
Junction coatings	Conformal coatings
Laminates	Foams
Moulding compositions	Gaskets
Miscellaneous applications	Glazing
Paints	Sealants
Pressure-sensitive adhesives	Surgical aids
Varnishes	Medical implants
Antifoamers	Mold making
Coagulants	Belting
Cosmetic and health product additives	Electrically conducting rubber
Dielectric media	Embossing-calendaring rollers
Greases	Fabric coating
Heat-transfer media	Foams
Hydraulic fluids	Fuel-resistant rubber parts
Lubricants	Laminates
	Medical implants

Table 5 (cont.)

LSR	HTV
Plastic additives	Molded parts
Polishes	Penetration seals
Surfactans	Surgical aids
Vibration damping	

Poly(ethylene glycol) (PEG)

Poly(ethlene glycol) (PEG), the most commercially important type of polyether, has the general formula as $H(OCH_2CH_2)_nOH$). PEG and poly(ethylene oxide) (PEO) are similarly in chemical structure with, in the sense, different molecular weights. PEG refers to oligomers and polymers with molecular weights below 20,000 g/mol [50], while PEO tends to have higher molecular weights. PEG and PEO are liquids or low-melting solids. Melting points of PEG are strongly dependent on their molecular weights. PEGs with the molecular weights upto 700 g/mol are colorless, odorless and viscous liquids with a freezing point at -10°C, while PEGs with higher molecular weight than 1,000 g/mol are wax-like solids and show melting points upto 67°C. PEGs are prepared by polymerization of ethylene glycol (Figure 9) and are commercially available over a wide range of molecular weights from 300 g/mol to 10,000,000 g/mol.

PEG is known as a neutral, water soluble and non-toxic polymer [51, 52]. It is frequently used for chemical modification of natural and artificial macromolecules for biomedical applications [50]. PEG is well dissolved in water, acetonitrile, chloroform, dichloromethane, dimetylforamide and benzene, but insoluble in diethyl ether and hexane. Another most common type of PEG is a monofunctional methyl ether PEG or methoxy poly(ethylene glycol) (mPEG) [53]. It is frequently used for chemical modification of natural and artificial polymers.

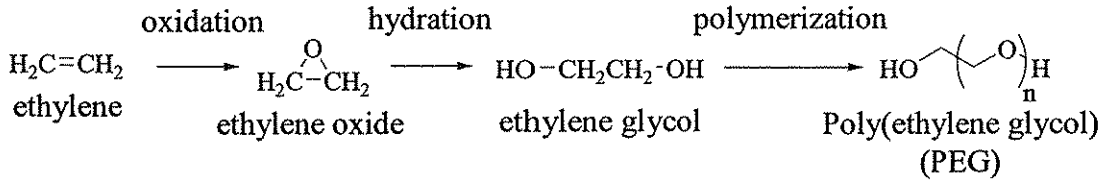


Figure 9 The process of acid hydrolysis for producing ethylene glycol and polymerization of PEG

Interpenetrating Polymer Networks (IPNs) [54]

When two or more polymers are mixed, the resulting composition can be called a multicomponent polymer material. There are several ways to mix two kinds of polymer molecules as shown in Figure 10. IPN comprises of two or more networks that are at least partially interlaced on a molecular scale but not covalently bonded to each other. It cannot be separated unless chemical bonds are broken. An IPN is distinctive from simple polymer blend, block or grafts in two ways: it swells but does not dissolve in solvent, and suppresses creep and flow properties.

1. History of IPNs

In 1914, the first invention of an IPN was discovered by Aylsworth. Researcher combined the new phenol-formadehyde compositions with nature rubber and sulfur. The next known discovery of IPNs was by Stuadinger and coworkers in 1941 [54]. They took sheets of crosslinked polystyrene or poly(methyl methacrylate) and swelled them with the same monomer to crosslink the structure in order to smooth the surface of the plastic sheets. The next invention of IPNs was coined by Solt in 1955. Researcher developed cationic-anionic ion exchange resins using suspension-sized particles. Soon after, the term "interpenetrating polymer networks" was invented by Millar in 1960 [54].

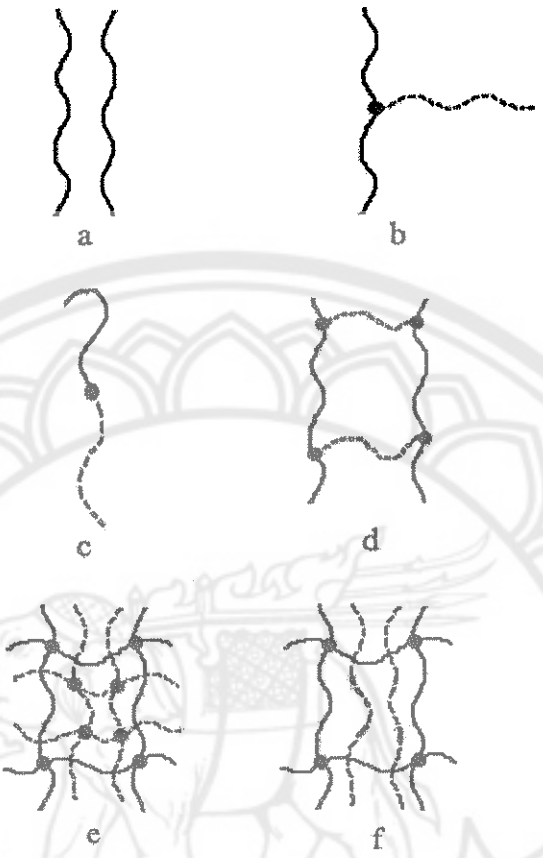


Figure 10 Six basic combinations of two types of polymers, a) polymer blend, b) graft copolymer, c) block copolymer, d) AB-graft copolymer, e) IPNs, and f) semi-IPNs.

2. Types of IPNs [54].

IPNs can be made in many different methods. Brief definitions of some important IPNs are following;

2.1 Sequential IPNs

Monomer, crosslinker and activator are swollen into a preformed network and polymerized in situ.

2.2 Simultaneous interpenetrating networks (SINs)

Monomers or prepolymers, crosslinkers and activators of both networks are mixed together. Two reactions are carried out simultaneously without interfering.

2.3 Latex IPNs

The IPNs are made in the form of latex, frequently with a core and shell structure. A variation is to mix two different latex and then form a film and then crosslink both polymers.

2.4 Gradient IPNs

Gradient IPNs are materials in which the overall composition of crosslink density of the material varies from location on the macroscopic level.

2.5 Thermoplastic IPNs

Thermoplastic IPN materials are hybrid between polymers blends and IPNs that involve physical crosslinks rather than chemical crosslinks. Thus, these materials flow at elevated temperature, similar to the thermoplastic elastomer, and at used temperature, they are crosslinked and they behave like IPNs.

2.6 Semi-IPNs [53]

Semi-IPNs comprises of one or more networks and one or more linear or branched polymer(s). It is envisaged as IPNs with penetration on a molecular scale of at least one of the networks by some of the linear or branched polymers.

Literature review

Chemical modifications of chitosan and CMC have been prevalently reported in many different ways, one of which is the formation of network structure. Interpenetration of polymers and particles into chitosan or CMC hydrogels is a method of choices that has widely gained much attention recently [55]. In this thesis, interpenetrating polymer networks (IPNs) were of particular interest. IPNs comprise of two or more networks interplaced on molecular scale but not convalently bonded. Due to the unique and intriguing properties of IPNs, they have been widely developed to use in a variety of applications [56]. In 1999, Jun Lee *et al.* have prepared IPN hydrogels by UV irradiation of poly(ethylene glycol) macromer (PEGM) with chitosan and used glutaraldehyde as a crosslinking agent. They reported that equilibrium water

content (EWC) of the hydrogels was in the range of 74–97%. The hydrogels revealed two glass transition temperatures (T_g), indicating the presence of phase separation in the IPN structure. The tensile strength and elongation at break of the IPN hydrogels in the swollen state ranged from 0.06 to 0.18 MPa and 18–48%, respectively [57].

Many IPN-based formulations for the control release of a variety of drugs have also been studied (Figure 11). Semi-IPN microspheres of acrylamide grafted on dextran (AAm-*g*-Dex) and chitosan (CS) have been synthesized by a water-in-oil emulsion method for controlled release of acyclovir with glutaraldehyde as a crosslinking agent [58]. Drugs were successfully encapsulated in the microspheres. Size of the semi-IPN microspheres ranged between 65–388 μm. According to UV spectrophotoscopy, up to 79.6% of acyclovir was encapsulated and its releasing period was extended to 12 h with accumulative release of up to 80%.

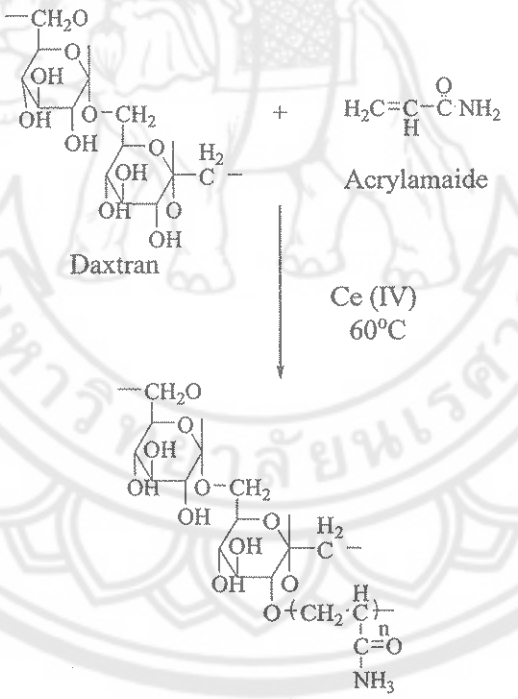


Figure 11 Schematic representation of the synthesis of AAm-*g*-Dex

In same year, Shiu Chih Wang, et al. used chondroitin sulfate (CS)-based hydrogels as a matrix for loading drugs. Two approaches for preparing the CS hydrogels were presented; directly crosslinking CS with poly(ethylene glycol) diglycidyl ether (EX-810), abbreviated as CS-EX and forming an IPNs, named as CS-

EX-IPN. The sol percents of CS-EX and CS-EX-IPN were 35.7±2.7 and 15.9±2.0, respectively. The values of compression modulus and effective crosslinking density of CS-EX-IPN were approximately 3.6 folds higher than those of CS-EX. Diclofenac sodium (DS) was used as a model drug, while bovine serum albumin (BSA) was used as a model protein. The result revealed that DS was immediately released from both CS-EX and CS-EX-IPN hydrogels, whereas BSA could be moderately controlled [59].

IPNs are also applicable in micro-electronic usage such as biosensors, chemical sensors and molecular sensors. Su Ryon Shin *et al.* reported the preparation of chitosan/polyaniline (PANi) semi-IPNs under different pH conditions with glutaraldehyde as a crosslinking agent. Electrical conductivity of the semi-IPNs increased with an increase in the PANi content. This was attributed to the interaction of the components in their structure, which rather reflected the overall charge transferring competency [60]. Xiandong Zeng *et al* have prepared semi-IPN hydrogels based on polyacrylamide (PAM) and chitosan and immobilized redox protein hemoglobin (Hb) in the gel structure. The cyclic voltammogram of Hb–PAM–chitosan on the modified glass carbon (GC) electrode signified that direct electron transfer between Hb and GC electrodes obviously occurred. The electron-transfer rate constant was about 5.51 s^{-1} in pH 7.0 buffers. The immobilized Hb showed good bioelectrocatalytic activity toward H_2O_2. The electrocatalytic current values increased with increasing concentrations of H_2O_2 in a wide range of 5–420 μM [61].

In medical applications, IPNs have been used for preparing antibacterial materials, e.g. silver nanocomposites. Murthy P.S.K. *et al.* synthesized semi-IPNs hydrogel–silver nanocomposite (SHSNC) with poly(acrylamide)/poly(vinyl pyrrolidone) (PAM/PVP) matrix [62] (Figure 12). PAM/PVP films were prepared *via* free radical polymerization with N,N-methylene-bisacrylamide (MBA) crosslinking agent. The films were immerged into $AgNO_3$ solutions containing ammonium persulfate/*N, N, N', N'*-tetramethylethylenediamine as a redox-initiating agent to obtain silver nanoparticles embedded in the hydrogels. An optimal formulation was achieved when high MBA concentrations were used and highly dispersed silver nanoparticles in the hydrogel networks were obtained.

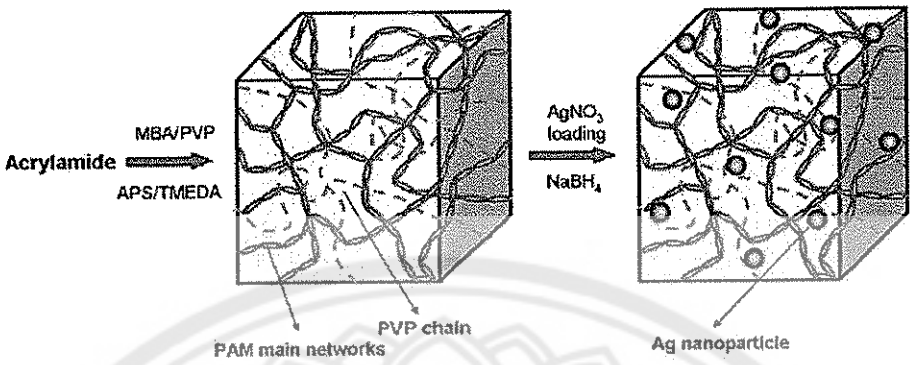


Figure 12 Schematic representation of *in situ* semi-IPN hydrogel–silver nanocomposites (SHSNC)

In 2005, Shu Huei Yu *et al.* have prepared semi-IPN membranes by crosslinking/grafting 6-O-carboxymethylchitosan (6-OCC)/waterborne polyurethanes (WPU) soft segments with glutaraldehyde or EGDE [63]. It was interesting to find that the miscibility of a 6-OCC/WPU composite membrane was improved after being converted into a semi-IPN membrane. Most importantly, antibacterial capability and thromboresistance of the WPUs were significantly improved by blending with 6-OCC and crosslinking/grafting with EGDE to form the 6-OCC/WPU semi-IPN membranes. These materials might be suitable for use as a biomaterial for blood-contracting devices. Soon after, Chen Yu and Tan Hui-min prepared CMC-*g*-poly(acrylic acid) (CMCTS-*g*-PAA) superabsorbent polymer through a graft polymerization of acrylic acid onto CMC chains and subsequently crosslinking. The rate of water absorption of the polymer was high up to 550% and swelling ratio of the polymer was pH-dependent [64].

In 2008, Shuibo Hua and Aiqin Wang prepared alginate-*g*-poly(acrylic acid)/sodium humate (NaAlg-*g*-PAA/SH) superabsorbent by graft copolymerization between sodium alginate, acrylic acid and sodium humate in aqueous solution, using *N*, *N'*-methylenebisacrylamide as a crosslinker and ammonium persulfate as an initiator (Figure 13). Equilibrium water absorbency of NaAlg-*g*-PAA/SH superabsorbent was significantly affected by the content of SH. The highest water absorbency was obtained when 10 wt% SH was incorporated. SEM investigation

revealed that the superabsorbent containing SH micropowers exhibited a coarse surface [65].

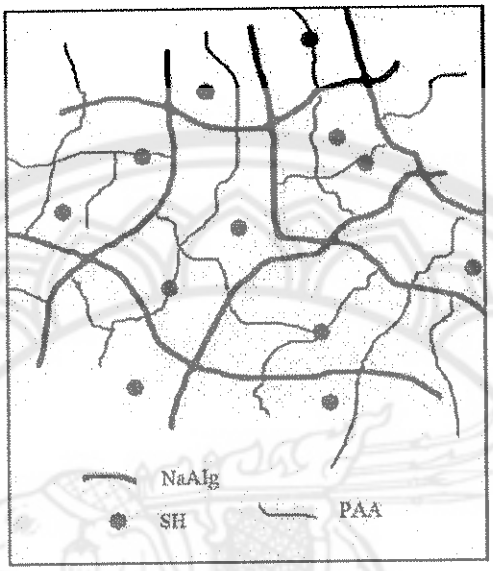


Figure 13 Schematic representation of the NaAlg-g-AA/SH superabsorbent

The use of water-soluble crosslinking agents for chitosan network formation has also been reported. Eric Welsh and Sheng Lin-Gibson have recently used hexamethylene 1, 6-di(aminocarboxysulfonate) (HDA), a reactive water-soluble diisocyanate derivative, as a crosslinking agent [66, 67]. HDA crosslinking agent was prepared from the reaction between hexamethylene diisocyanate (HDI) with $Na_2S_2O_5$ in water. Diisocyanate groups of HDI were reacted with a bisulfite of $Na_2S_2O_5$ to protect or block reactivity and to impart water solubility properties. While it is stable in acidic aqueous solutions with increased pH or temperature, the adduct readily reacts with amines, forming a urea linkage. This crosslinker remains soluble in water or alcohol, therefore, enables for facile processability of chitosan gel formations.