CHAPTER 1

GENERAL INTRODUCTION

For the last few decades, polymeric materials have emerged as unique class of materials due to their versatility and appeal with outstanding mechanical properties, tailorability, functional properties, environmental stability, ease of processing into customer-desired products and host of other desirable properties. Polymer science and technology in the new millennium are facing new challenges and opportunities. Exhilarating developments are expected in almost all existing areas. The developments in the area of biomedical field are quite amazing. Material science and the new field of nano technology have opened up several possibilities for the engineering of better and smaller devices not only for technological applications, but also for use in humans. Biomedical applications of polymers ranging from diagnostic appliances, prosthetics and stents to engineered biopolymers, is increasing rapidly world over. Polymers when used as implants are non-traceable without invasive procedures. A radiopaque polymer would offer the unique advantage of being traceable via routine X-ray imaging. Radiopaque materials open up a new outlook to various technological applications like biomedical, radiation shielding, toy manufacturing, plastic explosives etc.
1.1 BIOMATERIALS

A biomaterial can be defined as a material intended to interface with biological systems to evaluate, treat, augment or replace any tissue, organ or function of the body. The term biomaterial include all materials used for medical applications that are interfaced with living systems or other systems developed for extra corporeal use. The natural tissues in our body can get damaged due to diseases, trauma or aging. Allografts appears to be the ideal and logical materials for replacement. Shortage of organs for implantation and the need for chronic immunosuppression, however, make them less reliable. Therefore, a variety of other materials have been tried as biomaterials. These include metals, glasses, polymers, ceramics, carbon and composites of various combinations of these. They are used singly and in combination to form most of the implantable devices available today. Metals and alloys have high impact and tensile strength. Stainless steel, gold, titanium and cobalt alloys are the commonly used materials in this group. Ceramics and composites have good biocompatibility and corrosion resistance. Since polymers can be tailor-made to match the mechanical and physical characteristics of many parts of the body, they find maximum applications as biomaterials. Some of the most commonly used biomaterials and their applications are shown in table 1.1.
Table 1.1: Some of the most commonly used biomaterials and their applications

<table>
<thead>
<tr>
<th>Field</th>
<th>Applications</th>
<th>Material used</th>
</tr>
</thead>
<tbody>
<tr>
<td>Implants</td>
<td>Cardiovascular</td>
<td>Poly(ethylene terephthalate), Poly(tetrafluoroethylene)</td>
</tr>
<tr>
<td></td>
<td>Facial implants</td>
<td>Collagen, Silicones, Poly(glycolic acid)</td>
</tr>
<tr>
<td></td>
<td>Breast implants</td>
<td>Silicones, Polyurethanes</td>
</tr>
<tr>
<td>Dentistry</td>
<td>Dental waxes</td>
<td>Polyethylene, Poly(oxyethylene glycol)</td>
</tr>
<tr>
<td></td>
<td>Dental cements</td>
<td>Zn(_2)(PO)(_4), ZnO, Eugenol, Silicates</td>
</tr>
<tr>
<td></td>
<td>Restoratives</td>
<td>Alloys, Resins, Silicates</td>
</tr>
<tr>
<td>Devices</td>
<td>Sutures</td>
<td>Polypropylene, Teflon, Dacron</td>
</tr>
<tr>
<td></td>
<td>Pacemaker</td>
<td>Epoxy resins, Dacron, Silicones</td>
</tr>
<tr>
<td></td>
<td>Catheters/tubings</td>
<td>Poly(vinyl chloride), Teflon</td>
</tr>
<tr>
<td></td>
<td>Artificial heart</td>
<td>Polyurethanes, Silicone rubber</td>
</tr>
<tr>
<td>Orthopaedic applications</td>
<td>Artificial joints</td>
<td>Ultra high molecular weight polyethylene (UHMWPE)</td>
</tr>
<tr>
<td></td>
<td>Bone cements</td>
<td>Acrylic resins</td>
</tr>
<tr>
<td></td>
<td>Tendons, ligaments</td>
<td>Polyethylene, Silicones</td>
</tr>
<tr>
<td>Ophthalmology</td>
<td>Intraocular lenses</td>
<td>Poly (methyl methacrylate) (PMMA)</td>
</tr>
<tr>
<td></td>
<td>Contact lenses</td>
<td>Poly (hydroxyl ethyl methacrylate) (PHEMA)</td>
</tr>
<tr>
<td></td>
<td>Retinal surgery</td>
<td>Silicone rubber</td>
</tr>
</tbody>
</table>
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1.2 POLYMERS AS BIOMATERIALS

The polymers can be of natural origin, (commonly termed biopolymers) and/or synthetic origin, the latter being the most extensively used. They are used in medical equipments as packing materials and as a wide variety of disposable devices. The main reason for the extensive applicability of polymers is the availability of synthetic polymers in a wide variety of chemical compositions and physical properties, their ease of fabrication into complex shapes and structures, their easily tailored surface properties and favorable cost performance ratio. Thus compared to other materials, polymers are advantageous in several ways. They are,

*Easy to fabricate:* They can easily be fabricated into many forms of final usage, such as fluids, fabrics, films and solids.

*Compatible to tissues:* Many polymers bear a close resemblance to natural tissues such as collagen, which render them suitable for medical applications.

*Available with wide choice:* They are available with different properties, transparent ones being suitable for ocular implants, opaque for orthopaedic implants and as adhesive for replacing sutures.

*Non-corrosive:* Unlike many metals, polymers are non corrosive.

*Low in density:* The density of most of the polymers are closer to the density of the natural tissues.

Thus polymers constitute, by far, the broadest and most diverse class of biomaterials, making the medical market the fourth largest area of polymer application. The first medical application of polymers made use of commercially available ones, adapted as necessary. Although the science and technology of polymers for biomedical application is at an early stage of development, recent
progress has been dramatic. Polymers penetrate virtually every aspect of medicine, though the science of polymeric biomaterial is much more recent than that of other high molecular weight polymers. Only a few polymers have been specially designed for medical uses, e.g., hydrogels for soft contact lenses, poly (glycolic acid) for absorbable sutures, special ion exchange resins, semipermeable membranes and silicone rubber.

Hundreds of synthetic polymers are available. However, only ten or twenty of them are mainly used in medical device fabrications from disposable to long term implants. This is because, the success of a biomaterial in the body depends on factors such as material properties, design and biocompatibility and hence these aspects should be rigorously satisfied. Some of the polymers commonly used as biomaterials and their applications are shown in table 1.2.
### Table 1.2 Commonly used polymers and their medical applications

<table>
<thead>
<tr>
<th>Polymer</th>
<th>Applications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Polyethylene</td>
<td>Catheter tubes, films for sterile conditioning sacs, syringe pistons, needle covers</td>
</tr>
<tr>
<td>Polypropylene</td>
<td>Yarns for surgical sutures, films for sterile conditioning sacs, cast bodies for syringes, rigid nozzles, sterilizable vessels</td>
</tr>
<tr>
<td>Poly (vinyl chloride)</td>
<td>Blood bags, medical tubings, dialysis tubings</td>
</tr>
<tr>
<td>Polyurethane</td>
<td>Adhesives, emulsions, dental materials, suture materials, blood pumps</td>
</tr>
<tr>
<td>Poly(Methyl methacrylate)</td>
<td>Bone cement, intraocular lenses, hard contact lenses</td>
</tr>
<tr>
<td>Polycarbonate</td>
<td>Sterilisable feeding bottles, syringes, plasma vials, arterial tubules</td>
</tr>
<tr>
<td>Silicones</td>
<td>Dental prostheses, artificial ventricles</td>
</tr>
<tr>
<td>Polyamide (Nylon 6,6)</td>
<td>Packaging, hypodermic syringes, inhalator</td>
</tr>
<tr>
<td>Chitosan</td>
<td>Coating material, blood anti-coagulant, drug delivery, tissue engineering</td>
</tr>
<tr>
<td>Poly (vinyl alcohol) (PVA)</td>
<td>Drug delivery, particulate emboli</td>
</tr>
<tr>
<td>Poly (hydroxyl ethyl methacrylate)</td>
<td>Contact lenses, particulate emboli</td>
</tr>
</tbody>
</table>
Search for new biomaterials has expanded rapidly over the last few years. It is important to realize that successful application of a biomaterial is possible only if stringent requirements are met. Some of these are,

**Biocompatibility**: The material should not induce any undesirable or harmful effect such as blood clotting, allergic reaction, tissue death, inflammation, foreign body reaction etc.

**Physical properties**: Strength, elasticity, permeability etc. must fit within the application and should be maintained throughout the service life of the material.

**Manufacture**: It should be possible to fabricate, purify and sterilize the part without major hiccups.

Among these properties, the most important requirement of a biomaterial is its biocompatibility. Biocompatibility can be defined as the ability of a material to perform with an appropriate host response in a specific situation. Usually, compatibility of a new material is evaluated as far as possible, through a battery of in vitro tests and a follow-up of in vivo or ex vivo evaluation, using animal models.

Research on new polymeric biomaterials has expanded rapidly over the last couple of decades. It would be very helpful to have a technique for non-invasive evaluation of polymeric implants. This would put the researcher into a position from which it is relatively easy to make observations as a function of time without sacrificing the animal model. X-ray and ultrasound radiographic imaging techniques are the most commonly used non-destructive techniques to evaluate materials. The search for a non-destructive method of polymer evaluation has ended up to a new area of research, comprising of radiopaque polymers.

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1.3 RADIOPAQUE POLYMERS

X-ray and ultrasound depend on variations in density between a specimen and its surroundings. Based on casting shadows, radiographic imaging techniques incorporate the principle of radiopacity, which is the physical property of absorbing X-rays or reflecting ultrasound waves. Light materials are moderately radiopaque while heavy materials strongly absorb X-rays and produce good contrast. The ultrasound imaging approach, however, suffers from the fact that it has only moderate sensitivity. X-ray imaging being fast, reliable, convenient and non-destructive, is commonly used in clinical practice. A relatively new and perhaps more promising approach for non-invasive evaluation of the performance of a biomaterial is to impart radiopacity to such materials so that they can be monitored for their function and performance in a non-invasive manner.

Radiopacity is now considered as a desirable property of implants used in surgery as it follows the post-operative assessment of the fate of the implant using X-radiography. Radiopacity is widely acknowledged as a property of all intra oral materials including denture base materials, denture liners etc. Elastomeric impression materials, endodontic sealers, posts and restorative materials, direct filling restorative materials and resin cement luting agents are all radiopaque.

However, until recently, these techniques were not sufficiently sensitive to direct polymers so that the physical changes that occur in polymer implants could be observed. Polymers cannot be detected by imaging techniques because they mainly contain the elements such as carbon, hydrogen, oxygen, nitrogen and in some cases elements like silicon (e.g. silicon rubber). Consequently, polymers exhibit relatively low electron density, which render them radiolucent. Sharp images can be obtained only from materials of high electron density. Research into radiopaque polymers explore methods of increasing average electron density.
and specific gravity of polymers by incorporating heavy elements into these systems. One of the common practice is to introduce radiopacity via radiopaque fillers. Additives\textsuperscript{13-18} such as barium sulphate, zirconium oxide, bismuth halides are incorporated to achieve the necessary X-ray contrast when they are produced by molding, casting, extrusion etc. The incompatibility of inorganics such as barium, bismuth or silver with the polymer matrix often affect the physical and mechanical properties of the implant adversely. Moreover, the possibility of the inorganic ions leaching into the body fluid over long periods of time also causes a threat both from the stand point of the stability of the implant and the toxicity of the metal ions\textsuperscript{19}.

1.3.1 RADIO PACIFIERS

Radiopacifiers are the substances added to a polymer matrix to impart radiopacity. The following are the commonly used radiopacifiers:

1. Metal inserts such as fine wire, gold gauze or lead foil have been introduced into dental methacrylic resin.

2. Barium sulphate: It is the most widely used compound for dental resins and bone cements. It is very stable, less expensive and can be made in to different colours.

3. Bismuth compounds: It is more expensive than barium sulphate. It has higher density and may produce a brighter and sharper X-ray image than barium sulphate.

4. Tungsten: It is compatible with most polymers. It is more than twice as dense as bismuth and provides a high level of radiopacity. Loading levels of up to 95 % by weight are possible. Host compounds containing tungsten are dark grey in color, which limits coloring option.
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One of the most important versatile radiopacifier is triphenyl bismuth. It forms miscible and often optically transparent blends of high opacity with a wide range of polymeric materials including polystyrene, polyvinyl chloride, polyalkenes, polyacrylates and epoxy resins. Low molecular weight iodine compounds in transparent plastic materials and toys provide improved X-ray contrast. Incorporation of elements of high atomic mass to increase the average electron density and specific gravity of polymers is done in many ways.

Based on the preparation, radiopaque polymers are classified into three groups. They are radiopaque polymer blends, radiopaque polymer salt complexes and polymerization products of radiopaque monomers.

1.3.2 RADIOPAQUE POLYMER BLENDS

Radiopaque polymer blends are produced by incorporating the radiopacifying agents as a physical mixture with the polymer. The introduced agent can be a heavy metal, inorganic salt of a heavy element or an organic compound containing a heavy atom substituent. Barium sulphate is an additive commercially used for denture resins and bone cements to make them radiopaque. It does not affect the hardness, solubility or absorption of the resin and tissue implants of the material. But barium sulphate reduces the tensile strength and minimizes the modulus of elasticity. It was observed that polymers containing zirconium dioxide show a high degree of radiopacity than those containing barium sulphate. Metal inserts such as fine wire, gold gauze or lead foil may also be introduced into resins to make them radiopaque. Small quantities of inorganic salts have been added for obtaining radiopacity. Many simple high boiling aromatic and aliphatic halides have been added to the polymerization solution to make them radiopaque. The main drawback of these systems is that the radiopaque additives are not
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chemically incorporated into the resin. Many of the metal salts leach into the body fluids over a long time, which makes their radiopacity a temporary phenomenon.\textsuperscript{23}

1.3.3 RADIOPAQUE POLYMER-SALT COMPLEXES

Radiopaque polymer-salt complex systems are produced by the incorporation of a radiopaque heavy metal into an appropriate polymer ligand via chelation. The resulting systems are homogeneous and possess both polymeric and ionic character. X-ray imaging demonstrated that the radiopacity of these systems are high. Cabasso\textsuperscript{24} et al investigated polymers and monomers that can solubilize heavy metal salts such as barium bromide, bismuth halides, uranyl nitrate and lanthanides. Polymer salt complexes of bismuth tribromide and uranyl nitrate with acrylated polyphosphonates\textsuperscript{25} have been synthesized, where the phosphoryl group is believed to provide a strong coordinating site to the metal ion. Similar complexes with polymers containing carbonyl function have also been synthesized\textsuperscript{26}.

1.3.4 POLYMERIZATION PRODUCTS OF RADIOPAQUE MONOMERS

Polymerization products of radiopaque monomers are produced by the introduction of the radiopacifying element either electrovalently or covalently into the monomer unit prior to polymerization. Barium and zinc acrylates have been reported as radiopacifier and it can be copolymerized with methyl methacrylate (MMA)\textsuperscript{27}. However, the ionic nature of these resins leads to significant absorption of water and the slow hydrolysis of poly (zinc acrylates) leading to the loss of the opacifying atoms. The best method to produce radiopaque polymers is to synthesize reactive monomers having covalently bound heavy atoms and use these monomers as building blocks for new polymeric biomaterials that can exhibit intrinsic radiopacity. Such materials can offer vital advantages since no compromise can be made between the introduction of radiopacity on the one hand
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and the preservation of physico-mechanical properties on the other. The disadvantage of radiopaque system formed from covalently bound heavy element is its relatively high cost.

1.4 A REVIEW OF COMMONLY USED RADIOPAQUE SYSTEMS

1. Cyanoacrylic derivatives: Isobutyl 2-cyanoacrylate (IBCA) and N-butyl 2-cyanoacrylate

Isobutyl 2-cyanoacrylate (IBCA) rapidly found acceptance for embolic vascular occlusion, especially for the treatment of arteriovenous malformations (avm’s). The main advantage offered by this derivative is its low viscosity and rapid polymerization when in contact with vascular endothelium or ionic solutions such as blood. The injected fluid gets rapidly polymerized by forming a hard intravascular cast trapping blood element.

Besides an uncompleted biocompatibility evaluation for intravascular use, IBCA also exhibits some undesirable characteristics such as an exothermic reaction during polymerization, difficulty to control polymerization time, lack of visibility, possible premature polymerization inside the catheter and rendering control of implantation difficult or hazardous. To avoid premature polymerization, the use of 5% glucose solution to flush all ionic materials from the system are mandatory, as also modifying polymerization time. A chemically similar monomer (NBCA) was proposed as a fast polymerizing agent for the endovascular treatment of ‘avm’. This derivative showed a shorter polymerization time than IBCA by the addition of iophendylate oil or acetic acid.

In-vitro studies showed that the polymerization time was delayed by increasing the proportion of contrast medium ratio, which provided an optimal embolization material with good flow properties. Another acrylic derivative, the ethyl-
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cyanoacrylate was patented as an embolic material, but no major advantages were found\textsuperscript{28}.

A vascular graft catheter comprises highly radiopaque polyolefin compound, where the radiopaque material in the said compound is substantially uniformly dispersed and held within a polymer matrix. During the method, the first step is to heat low density polyethylene to its melting temperature. The amount of polyolefin is equal to 10 % by weight of the compound. Then an amount of radiopaque metal powder equal to 90 % by weight of the compound is added. The metal powder is preferably tantalum, tungsten, gold or platinum. Thereafter, an amount (at least 0.2 % by weight of the compound) of dispersing agent is added to polyolefin to form a mixture. The dispersing agent is preferably zinc stearate, aluminium stearate or calcium stearate. At last the mixture is mixed and cooled below its melting temperature to form the compound. Once the compound is formed, it can be cut into pellets and then is extruded into a tubular form for making tubular tip.

2. \textit{Methyl methacrylate Derivatives}

Methyl methacrylate derivatives with an average of twenty two ethylene units were synthesized and chelated with barium bromide. However, permanent radiopacity was not achieved with these derivatives and this limit the potential for their clinical application. Cation-chelating monomers were developed to achieve complete solubilization of heavy salts.

Blends of poly(methyl methacrylate) and heavy metal salts were developed by dissolving bismuth tribromide or sometimes bismuth chloride in MMA up to 40 % by weight. The high solubility of the salt resulted from the interaction between carbonyl group and bismuth because the electron donating monomer would readily interact with radiopacifying heavy metal.
Clear solutions of BiBr₃ could also be obtained with other monomer containing a carbonyl functional group. For eg. MMA /BiBr₃ mixture was polymerized to form solid resins. The presence of about 40 wt% of the salt decreased the molecular weight of PMMA from 1,20,000 to about 80,000 g/ml and slightly increased the glass transition temperature from 108° C to 123° C. PMMA-BiBr₃ resins develop opaqueness on contact with water. The influence of BiBr₃ content in PMMA on biocompatibility was tested and no sign to mutagenicity was revealed.

PMMA containing organo bismuth radiopacifying additive has also been reported. The X-ray contrast agent used was triphenylbismuth (PH₃Bi) and it was soluble in PMMA up to 70 %. A minimum of 23 % halogenated derivative was necessary to obtain the same radiopacity as the aluminum standard. Bismuth compound acts as a plasticizer and the glass transition temperature of PMMA was reduced. PH₃Bi is very resistant to moisture and water. Therefore it avoids leaching out in an aqueous environment. It is very stable to heat and air. PH₃Bi also shows lower toxicity as PMMA alone. Radiopaque derivatives could also be prepared using triphenyl bismuth and polystyrene.

Transparent, hard materials were obtained by copolymerizing MMA and styryldiphenylbismuth at 65°C with benzoyl peroxide as initiator. The synthesized products had a glass transition temperature of 100-110° C, close to that of PMMA because the heavy metal was a part of the backbone of the product. Thus, the thermal and mechanical properties of the polymers, in comparison to materials containing heavy metal components as additives only, were improved. Permanent chemical incorporation into the polymer structure prevented the leaching out of the heavy metal X-ray contrast agent in any kind of solvent. Identical copolymerization could be obtained with other monomers such as styrene or other vinyl monomers²⁹.
Another approach to opacify PMMA has been patented and was achieved by incorporating bromine into the PMMA resin. The synthesis of 2,3-dibromopropyl methacrylate was carried out by refluxing methacrylic acid and 2,3 dibromopropanol in toluene. The product obtained was a colorless liquid with a boiling point 82 - 86°C. It is possible to polymerize the 2,3-dibromopropyl methacrylate to obtain a homopolymer that possess a high bromine content (55.9 wt%) and hence highly satisfactory radiopacity, but is also highly brittle. To improve the mechanical properties of the brominated polymer, copolymerization of poly (2,3-dibromopropyl methacrylate) with MMA at 70°C using azoisobutyronitrile as initiator was employed. The synthesized copolymers had a cross linked structure and their equilibrium water absorption decreased with increasing content of poly (2,3-dibromopropyl methacrylate). The flexural strength decreased continuously while the elastic modulus increased proportionally to the content of the brominated polymer. The loss of tensile strength and impact strength was minimized until 60% of the bromination.

Synthesis and polymerization of iodine containing methacrylate have been reported. Variable radical polymerization behavior was exhibited when comparing similar methacrylic monomers. For example, 2,3,6-triiodophenyl methacrylate showed a poor tendency to homopolymerization and gave only oligomeric product, while 2,3,5-triiodobenzoyloxy alkyl methacrylate yielded polymers with number average molecular weight about 58,000 - 1,47,000 under similar conditions. The 2,4,6-triiodophenyl methacrylate reduce the MMA polymerization and thus decreased the number average molecular weight of the formed polymers.
1.5 APPLICATION AREAS OF RADIOPAQUE POLYMERS

Manufacturing industries of plastics, biomedical polymers, defense materials etc. explore the properties of radiopaque polymers extensively are indicated below.

- In biomedical field it is used for the preparation of implants, catheters, medical adhesives and in dentistry for prosthetic applications such as denture or restorative resins
- It is also used for the detection of changes within the body organs such as the kidneys, blood vessels, heart or gastrointestinal system
- Radiopaque compounds are also used to produce shielding components to enclose radiation generating sources
- It is used in toy manufacturing to enable radiographic detection of toys swallowed by children
- Radiopaque polymers are used in plastic explosives, which cannot be detected by conventional X-ray techniques. Incorporation of heavy metal salts into these systems can facilitate their detection for security
1.6 NATURAL POLYMERS USED FOR THE PRESENT STUDY

In this thesis an attempt has been made to prepare radiopaque, biocompatible polymers and to explore their radiopaque properties. To this end, we use chitosan and natural rubber as matrix polymers. The chemistry and the applications of these two are reviewed in the following sections.

1.7 CHITIN AND CHITOSAN

Nature has chosen two different but related polysaccharides to provide structure and integrity to plants and animals like crustaceans and insects. Plants have cellulose in their cell walls while insects and crustaceans have chitin in their shells. Cellulose molecules are large chains of glucose units while chitin molecules are large chains of N-acetyl glucosamine units. Cellulose and chitin are two of the most abundant biopolymers on earth. Chitin is a highly insoluble material resembling cellulose in its solubility and low chemical reactivity. It may be regarded as cellulose with hydroxyl at position C-2 replaced by acetamido groups. The principle derivative of chitin is chitosan. It is formed through N-deacetylation of the chitin molecule. The structures of chitin, chitosan and cellulose are shown in figure 1.1.
Thus chitin is a nitrogenous polysaccharide which is white, hard and inelastic. It is found in the outer skeleton of insects, crab, shrimp and lobsters and in the internal structure of other vertebrates. Chitin has a crystalline structure and it constitutes a network of organized fibers. Chitosan also occurs naturally in some fungi but its occurrence is much less widespread than that of chitin.
1.7.2 PROCESSING OF CHITIN AND CHITOSAN

Chitin is widely distributed both in the animal and plant kingdom. In animals, the most readily associated sources are in the shells of crustaceans and mollusks, the backbone of squids and the cuticle of insects. Japan is the major manufacturer of chitin with an annual production of about 500 tones. Serious environmental problems caused by prawn shell waste can be avoided by using it as a raw material for the production of chitin and its derivatives. In addition to control environmental pollution, it is a valuable recourse for more employment and additional income.

In crustaceans chitin is found as a constituent of a complex network with proteins into which calcium carbonate deposits to form the rigid shell. The interaction between chitin and protein is very intimate with covalent bonding, and in essence is a polysaccharide protein complex. The processing of crustacean shells mainly involves removal of proteins and dissolution of calcium carbonate which is present in crab shells in high concentrations. The resulting chitin is deacetylated in 40 % sodium hydroxide at 120 °C for 1-3 h (figure 1.2).

![Figure 1.2: Deacetylation of chitin](image-url)
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Deproteinisation is done with dilute alkali and demineralization with dilute acids. Variations in the reagent used and their concentration, as well as the time and temperature of treatment determine the quality and performance of the product.

1.7.3 PHYSICOCHEMICAL CHARACTERISTICS OF CHITOSAN

Most of the naturally occurring polysaccharides such as cellulose, dextran, pectin, agar etc. are neutral or acidic in nature, while chitin and chitosan are highly basic polysaccharides. Their unique properties include polyoxysalt formation, ability to form films, chelate metal ions and optical structural characteristics.

1.7.3.1 Degree of N-acetylation

Chitosan is characterized by either the degree of acetylation (DA), which corresponds to the N-acetylamine groups or the degree of deacetylation DDA (DDA=100-DA), D-glucosamine groups. The degree of acetylation has an influence on all the physicochemical properties (molecular weight, viscosity, solubility etc.). Many techniques have been tried to determine the degree of acetylation more precisely which include IR spectroscopy, pyrolysis gas chromatography, gel permeation chromatography and UV spectrophotometry. The most appropriate technique for rapid characterization seems to be IR spectroscopy.

1.7.3.2 Molecular weight

The knowledge of average molecular weight of chitin and chitosan is very important for industrial uses and for critical applications fields. Although the primary structure of chitosan comprises a backbone of (1-4)-β-D-glucosamine residues randomly acetylated to various extents, the name chitosan is in fact a collective term for deacetylated chitin differing in terms of crystallinity, optical characteristics, degree of deacetylation, impurity content and average molecular
weight. Chitosan molecular weight distribution has been obtained using HPLC\(^{46}\). Viscosity measurements are widely used. More recently gel permeation chromatography (GPC) or gel filtration chromatography (GFC) has been applied to study the molecular weight.

1.7.3.3 Solubility

Chitin is highly hydrophobic in nature and is insoluble in common organic solvents as well. It is soluble in hexafluoroisopropanol, hexafluoroacetone, chloroalcohol in conjugation with aqueous solution of mineral acids and dimethyl acetamide containing 5 % lithium chloride\(^ {47}\). Chitosan, the deacetylated product of chitin, is soluble in dilute acids like acetic acid, formic acids etc. Hydrolysis of chitin with concentrated acids produces relatively pure amino sugars, D-glucosamine. The nitrogen content in chitin varies from 5 to 8 % depending on the extent of deacetylation.

In fact, chitosan is soluble in dilute acids on account of protonation of free amino groups. As in all polyelectrolytes, the dissociation constant of chitosan is not constant but depends on the degree of dissociation at which it is determined. The solubility of chitosan depends on its degree of dissociation.

1.7.3.4 Crystallinity

On the basis of the crystalline structures, chitin is classified into three forms: \( \alpha, \beta \) and \( \gamma \)-chitins (hydrated, anhydrous crystal, and non-crystal). These forms can be examined easily by measuring the X-ray powder diffraction pattern of a chitosan sample\(^ {48}\). The modified forms of chitosan are less crystalline than pure deacetylated chitosan.
1.7.4 DERIVATIVES OF CHITOSAN

1.7.4.1 Chemical modification of Chitin and Chitosan

Chitosan can carry a large number of amine groups on its chain and thus can form multiple complexes. At higher pH levels (over 4) it can form complexes with colorants and heavy metals. The presence of the pair of free electrons of the amine groups is assumed to be the origin of the dative bonds, an idea confirmed by the observation of a much weaker fixation in chitin. Several chemical modifications can be done on chitin and chitosan. These are acylation, aldimination, carboxymethylation, sulphation, complexation with metal cations and some miscellaneous reactions.

1.7.4.2 N-acetylation

N-acetylation of chitosan leads to fully N-acetylated chitin. Complete N-acetylation may be achieved in 3 minutes at room temperature using a highly swollen chitosan in organic aprotic solvents. Chitosan boiled with large excess of hexanoyl or dodecanoyl chlorides in dry pyridine or chloroform gave fully acetylated derivatives. An aspirin carrier is prepared by the reaction of chitosan with 2-acetoxy benzoic anhydride.

1.7.4.3 Carboxylate derivatives

The insertion of carboxylic functions in chitosan has been widely studied. O-carboxymethylation is achieved with monochloroacetic acid and sodium hydroxide. Carboxymethylation is supposed to proceed preferentially at C-6 as implied from the results of backbone hydrolysis. Crosslinked carboxymethyl chitin or chitosan show high capability of separating bovine serum fibrinogen and albumin. Muzarelli et al demonstrated that N-carboxymethylation could be obtained first, reacting the amino group on chitosan with glyoxylic acid which
yields the intermediate, aldimine. Subsequent reduction gives N-carboxymethyl chitosan that is readily soluble in water for the whole pH range. The structure of Carboxymethyl chitosan is shown in figure 1.3.

![Figure 1.3: Carboxymethyl chitosan](image)

1.7.4.4 Sulphation

Sulphation of chitin and chitosan has been one of the most attractive modifications owing to the possibility of preparing anticoagulant polysaccharide in view of the structural similarity to heparin. For sulfitation various reagents have been used including conc. H₂SO₄, SO₃/pyridine, SO₃/SO₂ and chloro sulfonic acid. The trityl-chitin/chitosan intermediate has also been used to develop chitin and chitosan sulphates that have been investigated for their anti-HIV activity. In chitin, hydroxyl groups are sulphated, whereas with chitosan, sulphation occurs at both hydroxyl and amino groups. The sulphur trioxide-pyridine complex is selective for sulphation of chitosan amino groups.

1.7.4.5 Phosphorylation

The insertion of phosphate functions into chitosan has made it possible to develop a wide variety of polymers, soluble and insoluble, which complex and fix metals such as nickel, zinc or cadmium. The phosphorylation reaction of chitin and
Chitosan in \( \text{P}_2\text{O}_5\)-methane sulphonic acid system was found to be very efficient. Chitin and chitosan phosphates can easily be made insoluble by the cross linking reaction with adipoyl dichloride. A novel water soluble chitosan derivative carrying phosphonic groups was also synthesized. Chitin and chitosan phosphates adsorb alkaline earth metals and their ions more strongly than that of chitin and chitosan.

1.7.5 APPLICATION AREAS OF CHITIN AND CHITOSAN

The driving force for much of the excitement surrounding chitin and chitosan are the potential applications that the material can be used for. Table 1.3 lists potential applications for chitin, chitosan and their derivatives.

<table>
<thead>
<tr>
<th>Application</th>
<th>Specific use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Water treatment</td>
<td>Coagulating agents for polluted water, removal of metal ions</td>
</tr>
<tr>
<td>Agriculture</td>
<td>Plant elicitor, antimicrobial agents, plant seed coating</td>
</tr>
<tr>
<td>Textile, paper industry</td>
<td>Fibers for textile and woven fabrics, paper and film</td>
</tr>
<tr>
<td>Biotechnology</td>
<td>Chromatography, packing, enzyme immobilizing material</td>
</tr>
<tr>
<td>Food/health supplements</td>
<td>Natural thickeners, food additives, Filtration and clarification, Hypocholesteromic agents (slimming agents)</td>
</tr>
<tr>
<td>Cosmetics</td>
<td>Ingredients for hair and skin care</td>
</tr>
<tr>
<td>Biomedical</td>
<td>Wound dressings, absorbable sutures, anticoagulant or antithrombogenic materials, homeostatic agents, drug delivery, gene delivery</td>
</tr>
</tbody>
</table>

Table 1.3: Potential applications for chitin, chitosan and their derivatives
1.7.5.1 Biomedical applications of chitin

Chitin as a biomaterial can be exploited in two main matters, as a biostable material or as a biodegradable material, chitosan being a safe and friendly substance for the human organism. Medical and pharmaceutical applications can easily be worked out with joint efforts from specialists in various fields. As medical devices, the applications of chitin can be conveniently divided into two classes, external and internal. As an external device, chitin is used for making external communicating devices that come into contact with intact natural channels of the body such as the eye, vagina, and the gastro-intestinal tract and those that breach the body surface or contact blood such as in intravenous catheters or conduit for fluid entry. Examples of chitin applied in external medical devices are contact lenses, wound dressings, haemostatic agents and coating of the inner lumen of blood contacting tubing. Internal devices are normally implants that are targeted for bone, tissue, tissue fluid and blood. Examples of internal medical device applications of chitin include orthopedic implants such as bone pins, plates and cements, tissue engineering scaffolds, systemic anti coagulants, drug delivery components and gene delivery vehicles. Outlined below are some of the biomedical applications of chitin and chitosan.

1.7.5.2 Drug Delivery

Drug delivery is concerned with combining of drugs with other constituents to provide dosage forms suitable for administration to the patient. The non-drug constituents serve roles such as bioprotection of the drug or the body from the drug and absorption enhancement of the drug. The active agent i.e. the drug is combined with a polymeric material. Common requirements for the polymeric material are compatibility with the active agent, non toxicity, stability, sterilizability and biodegradability. An assessment of these factors identifies chitin
as a candidate that fulfills the basic requirements. All interesting properties of chitin and its derivatives, predominantly chitosan, make this natural polymer an ideal candidate for controlled drug release formulations. The most popular method of administration by far is oral where micro particulate, liposome, solution, vesicle, film coated, tablet and capsule forms are known. Microspheres and their more recent successor nano spheres are a popular method of effecting drug delivery systems useful in parenteral applications. Hydrogels based on chitin and chitosan have been widely used in controlled release systems. The pH sensitive hydrogels have potential use in site-specific delivery of drugs to specific regions of the gastro intestinal tract and have been prepared for low molecular weight and protein delivery. Chitosan/polyether interpenetrating network (IPN), hydrogel, semi IPN hydrogels of β-chitin/polyethylene glycol, chitosan/gelatin hybrid polymer network etc. were reported in controlled drug delivery.

1.7.5.3 Gene delivery

Mumper et al. were the first to describe the potential of chitosan as a gene carrier. The low toxicity of chitosan and its nature makes it attractive for gene delivery purposes. In early studies, chitosan has been shown to bind nucleic acids, and it is known that chitosan may actually be endocytosed into the cell. The hybrid DNA-chitosan systems can be classified into two categories, they are chitosan-DNA complexes and nanospheres.

1.7.5.4 Cholesterol and overweight lowering

Chitosan is an effective in lowering total and LDL cholesterol. Chitosan appears to be active in humans at rather low doses, with as little as 1.2 g per day producing significant reductions in serum cholesterol. In vitro studies show that chitosan has been reported to bind bile acids with approximately one-half or equal capacity of cholestyramine, a strong synthetic anion exchanger. Saturated fats are particularly
implicated in raising LDL levels, which increase the risk of developing
atheroscleroses, heart attack and stroke. The liver constantly endeavours to clear
out the bad cholesterol by dumping it into the intestine.

1.7.5.5 Dressing of wounds

Modified chitin has been administered to humans in the form of dressings for
wounded soft and bone tissues. Chitin has been found to have an accelerating
effect on the wound healing process. The choice of chitosan was to preserve the
good antigen affinity property after sterilization. Regenerated chitin fibers, non-
woven mats, sponges and films increase the wound healing process by over 30%.
Chitin can also be used as a coating on normal medical materials. Standard silk
and catgut sutures coated with regenerated chitin or chitosan show wound healing
activities. Surgical gauze coated with regenerated chitin demonstrates a
substantially greater amount of activity than uncoated control group. Gel like
pastes comprising chitosan blended hydrocolloid materials such as polysaccharide
gums has also been described as wound filling compositions.

1.7.5.6 Treatment of burns

Chitosan is a very attractive candidate for burn treatment. Chitosan has the ability
to form tough, water absorbent and biocompatible films with good oxygen
permeability. These films can be formed directly on the burn by application of an
aqueous solution of chitosan acetate. The solution although acidic, provides a cool
and pleasant soothing effect when applied to the open wounds of burn patients.
Additionally chitosan films have the ability to absorb water and are naturally
degraded by body enzymes. This means that chitosan need not be removed. Chitin
can also be prepared in the water soluble form by carefully deacetylating to about
50 % N-acetyl content. Fluid absorbing chitosan has also been proposed as
wound dressing material.
1.7.5.7 Ophthalmology

Chitosan possesses optical clarity, mechanical stability, gas permeability (particularly towards oxygen), wettability and immunological compatibility. Contact lenses are made from partially depolymerized and purified squid pen chitosan by spin casting technology. The contact lenses prepared from chitosan are clear, tough and possess other required physical properties such as modulus, tensile strength, tear strength, elongation, water content and oxygen permeability. The antimicrobial and wound healing properties of chitosan along with an excellent film capability make chitosan suitable for development of ocular bandage\textsuperscript{91}.

1.7.5.8 Chitosan as a fat trapper

Chitosan attaches itself to the fat in the stomach before it is digested, thus trapping fat and preventing its absorption by the digestive tract. Fat, in turn, binds to the chitosan fiber forming a mass which the body can't absorb and is eliminated by the body. Chitosan\textsuperscript{92,93} fiber differs from other fibers in that it possesses a positive ionic charge, which gives it the ability to bind chemically with the negatively charged lipids, fats and bile acids.

1.7.5.9 Chitosan as a new haemostatic agent

More recently Malette\textsuperscript{94} et al described the use of a new haemostatic agent such as N-hexanoyl and N-octanoyl chitosan which can be used even under most severe conditions of anticoagulation. It is apparently a safe agent which does not adversely affect graft healing.
1.7.5.10 Blood anti-coagulants (heparinoids)

Chitin and chitosan sulphates have blood anticoagulant and lipoprotein lipase (LPL) releasing activities. Chitin 3,6-sulphate shows about two-fold anticoagulant activity and 0.1 fold LPL-releasing activity over those of heparin.  

1.7.5.11 Anti-bacterial agents

The growth of Escherichia coli was inhibited in the presence of chitosan (more than 0.025 %). Chitosan also inhibits the growth of Fusarium, Alternaria and Helminthosporium. The cationic amino groups of chitosan probably bind to anionic groups of these microorganisms, resulting in growth inhibition.

1.7.5.12 Bone substitutes

Bone is largely made up of two components, an intimate combination of collagen and calcium hydroxyapatite. Chitin has been applied both in pure form as well as in combination with calcium compounds in orthopedic applications. Maeda et al were one of the first to use chitin in the form of braided filaments, rods and powders. These substitutes are found to be potentially suitable for sutures and temporary artificial ligaments for the knee joint. Borah et al studied the bone induction properties of N-acetyl chitosan. Chitosan was found to be better than the control and concluded that chitosan had osteogenic properties. More recently Chitosan–hydroxyapatite nano composites have been prepared and were found to be mechanically flexible and promoted bone formation.

1.7.5.13 Implants

Implantable devices are expected to be intelligent, nontoxic, nonthrombogenic, non carcinogenic and easily implantable with adequate storage capacity and possess drug stability, biodegradability and sterilizability. Khor and Lim discussed various applications of chitosan implants in a recent review. Chitin and chitosan
have been used in orthopedic and periodontal applications\textsuperscript{98,99}. Microspheres based on chitosan implants were prepared by cross linking with genipin and glutaraldehyde\textsuperscript{100}. Recently\textsuperscript{101} chitosan and sodium hyaluronate implants for controlled release of insulin were studied.

### 1.8 NATURAL RUBBER

Of all materials provided by nature for man to use as a material of construction, natural rubber is unique. Today there are many man made rubbers but natural rubber still plays a substantial role on the world's industrial stage, a story very different from that of many other natural materials which are challenged by synthetics. Natural rubber\textsuperscript{102,103} (NR) (cis, 1, 4-polyisoprene) occurs in over 200 species of plants. The \textit{Hevea brasiliensis} tree accounts for over 99\% of the world's natural rubber production, which in 1986 amounted to over 4x10\textsuperscript{6} tonnes. Historically, rubber as a material was known to and used by man as early as the sixth century, as excavations subsequent to the discovery of America have revealed.

Fresh Hevea latex, from which natural rubber is obtained contains about 25-45\% rubber hydrocarbon and 5-6\% non rubber substances such as amino acids, proteins, carbohydrates, neutral and polar lipids, and inorganic salts; the remainder being water. The high molecular weight and the presence of non rubber substances may give rise to inside reactions; such as cross linking, degradation, cis-trans isomerization during chemical reactions, and finally the reduction in activity. The non rubber substances also prevent the occurrence of certain reactions that can be carried out with synthetic cis-1, 4-polyisoprene. In its chemical reactions it behaves as a simple trialkylethelyne. However the reactions are influenced by two factors compared to the reactions of simple olefins. The first is the polymeric nature of natural rubber, which has a weight average molecular weight of
$1 \times 10^6 - 2 \times 10^6$. This gives rise to difference in its solubility and viscosity. The second factor is the chemical composition of natural rubber.

1.8.1 DERIVATIVES OF NATURAL RUBBER

Before the 1960’s, interest in the chemical modification of natural rubber focused on new materials with unusual properties. In the last 20 years however, more emphasis has been placed on modifying natural rubber in a controlled way without altering its strength properties. A great number of chemical derivatives have been prepared from natural rubber, but only a few have attained commercial significance, mainly because of the high cost of manufacture.\textsuperscript{104}

The natural rubber derivatives are divided into four (i) those resulting from bond rearrangements without the introduction of new chemical groups (ii) those resulting from the attachment of pendent functional groups to the natural rubber molecule by olefin addition or substitution reactions (iii) those obtained by grafting of a different polymer at one or more points along the natural rubber molecule and (iv) other derivatives.

1.8.2 Bond Rearrangement Reactions

1. Isomerized rubber

The 1, 4 poly isoprenes occur as isomers with different cis-trans ratios, ranging from the 100 % cis structure of natural rubber to the 100 % trans structure of gutta-percha.
The first successful cis-trans isomerization of natural rubber was reported in 1959. The transformation can be carried out with the help of catalysts on natural rubber in the form of a solid, solution, or latex. Isomerization takes place when thin film, sheets, or crumbs are heated with sulphur dioxide above 100 °C.

In commercial practice, butadiene sulfone is used, which produces sulphur dioxide in situ. The reaction with sulphur dioxide does not involve free radicals and probably proceeds by an "on-off" reaction at the double bonds.
2. Cyclized Rubber

Cyclized rubber, the first chemically modified derivative of natural rubber, is a hard, resinous product obtained by treating the rubber with strong acids or Lewis acids. Sulphuric acid, titanium chloride, ferric chloride, stannic chloride, p-toluene sulfonic acid and its chloride, and boron trifluoride etc. have been used. Cyclizations are carried out on solid rubber, solutions or latex, depending on the catalyst. Cyclized rubber has the same empirical formula \((C_3H_5)\) as polyisoprene, but has a lower degree of unsaturation. Cyclization proceeds via the carbenium ion mechanism. The protonated structure may cyclize to one ring, two rings, or more rings before deprotonation. The deprotonation reaction may result in tetra-tri or di substituted double bonds.

Cyclized rubber is also manufactured by adding concentrated sulphuric acid to latex stabilized with nonionic or cationic surfactant. The final concentration of acid in the aqueous phase should be at least 70 % by weight. The mixture is heated at 100\(^\circ\) C for 2 h under careful temperature control. The cyclized rubber latex is coagulated by pouring into aqueous alcohol or boiling water, and then filtered, washed and dried. A cyclized master batch can be produced by mixing cyclized and uncyclized lattices before coagulation.
3. Hydrogenated Rubber

Complete hydrogenation of natural rubber would give an altering copolymer of ethylene and propylene.

Figure 1.6: Hydrogenation of natural rubber
Hydrogenation without degradation has been accomplished with the help of nickel catalyst on kiselguhr at 170-180° C under a pressure of 1.5 - 2 MPa. However, the catalyst is easily poisoned by impurities and separation of catalyst is difficult. Hydrogenated rubber is more crystalline and has a slightly higher glass transition temperature than natural rubber. It can be vulcanized with the conventional systems. The vulcanizates show good ozone resistance at a high degree of hydrogenation.

4. Hydrohalogenated rubber

Hydrogen chloride adds readily to natural rubber to give the derivative rubber hydrochloride. The addition follows Markonikoff's rule but is accompanied by some cyclization. The product has a syndiotactic configuration and has slightly lower chloride content than the theoretical amount.

Rubber hydrochloride is a highly crystalline, tough, semi-elastic and film-forming. Its solubility is similar to that of chlorinated rubber. It loses hydrogen chloride on heating to about 100° C. The addition of hydrogen bromide proceeds like the addition of hydrogen chloride, rubber hydrobromide has been obtained as a powder but it is unstable.

5. Alkyl halogenated Rubber

Polyhalogen derivatives of alkanes containing at least one bromine atom add to rubber in the presence of peroxide. Carbon tetrabromide and trichlorobromomethane show high reactivity. The derivatives are prepared by adding the halogen compounds together with tert-butyl hydro peroxide to the stabilized latex. The reaction is allowed to proceed for about three days at room temperature. The products are elastic and vulcanizable and show some flame resistance. The best combination of physical properties and flame resistance is exhibited by a product containing 15 - 20 % by weight of the halogen compound.
The latex derivative\textsuperscript{106} is suitable for the production of rubber-bonded hair pads and flame-resistant latex form for spreading on carpets or fabrics.

6. Epoxidized Rubber

Natural rubber can be epoxidized in solution or in the latex stage by peracids. The reagent may be conveniently prepared \textit{in-situ} to avoid side reactions. The early materials were probably contaminated with products of ring opening reactions. In the presence of strong mineral acids at low epoxidation, diols are formed. In the presence of free acids at high epoxidation and high temperature, the hydroxyl group attaches to an adjacent epoxide group to give a substituted furan. This reaction can continue along the chain to give a polymeric 1,5-disubstituted furan structure of various lengths.

Epoxidized natural rubber is prepared from latex with performic acid generated \textit{in-situ}. The latex is stabilized with a nonionic stabilizer and formic acid and hydrogen peroxide are added. The reaction is carried out at 30-65\degree C for different periods of time, depending on the degree of epoxidation required. The epoxidized latex is washed and dried. The acid is neutralized with base before or after coagulation.

7. Halogenated rubber

Natural rubber has been halogenated (e.g. chlorinated); the reaction is complex. Fully chlorinated natural rubber contains about 65 \% chlorine, the empirical formula of which is C\textsubscript{6}H\textsubscript{4}Cl\textsubscript{13.5}. This suggests that the chlorination reaction involves more than one isoprene unit and since the products are soluble, cyclization rather than cross-linking is indicated. Studies by Bloomfield\textsuperscript{107} showed that light, oxygen and peroxides did not affect the rate of reaction, which would, therefore, seem not to be of the free radical type. He also showed that the reaction occurred in three stages represented empirically by the following equation.
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In the first stage it was shown that one molecule of hydrochloric acid was liberated for each molecule of chlorine absorbed, and there was a considerable drop in the unsaturation of the rubber. Since a simple substitution reaction should not reduce unsaturation, this suggests that at least one rearrangement process is occurring such as cyclization. The ultimate structure of chlorinated natural rubber is not known, but one suggested structure is as follows.

The intrinsic viscosity of chlorinated rubber is much lower than that of NR for a given molecular weight. This suggests a more compact molecule, may be a cyclized structure rather than a linear one. Chlorinated rubber requires plasticizer to reduce the brittleness of the film. Choice of plasticizer gives the possibility of
matching the protective quality of the chlorinated rubber finish. The resistance of chlorinated rubber decreases as the temperature is increased. Chlorinated rubber finds various applications in paint and lacquers, moisture proofing, adhesives and heat insulation.

Bromination of polyisoprene appears to be less complicated. If bromine is passed into a solution of rubber in chloroform in the temperature range of 0 -40 °C the reaction is largely additive to give \( \text{C}_3\text{H}_5\text{Br}_2 \)\(_n\) although some substitution may occur. Different results are obtained by the use of N-bromosuccinimide. This reagent is used for the specific purpose of brominating alkenes at the allylic position. In natural rubber this type of bromination proceeds via free radical intermediates to give products substituted in the allylic position. Side reactions are said to lead to cyclization or cross linking.

Fluorine reacts very violently and destructively with rubber and product containing 30 % of fluorine has been obtained and these are quite rubbery and can be used for gaskets in fluorine generators and fluorine lines.

1.8.3 APPLICATION AREAS OF NATURAL RUBBER

With its wide range of properties, natural rubber can be used in a large variety of applications. Despite this the share of natural rubber in the elastomer market has decreased progressively since World War II. This is partly due to the higher price of natural rubber relative to SBR and partly due to inadequate supplies. The increase in the share of natural rubber in the last few years is due to the large switch to radial tires in the United States and elsewhere.

1. Tires

In passenger-car-radial-ply tires, natural rubber is used in the carcass as well as the sidewall; the latter due to the superior fatigue resistance and low heat build up of
natural rubber. In commercial vehicles, the amount of natural rubber used increases with the size of the tyre. In large earthmover tires, for example, almost 100% natural rubber is used due to the requirements of low heat generation and high cutting resistance. Natural rubber is used in blends with halo butyl rubbers in the inner liner of tubeless tires.

2. Mechanical Goods

These include a large variety of products such as hose, conveyor belts, rubber linings, gaskets, seals, rubber rolls, rubberized fabrics etc. In these products, the choice of elastomer is made on the best compromise between price and performance. Natural rubber is used in some products only because it has certain properties that cannot be matched by any other rubber.

3. Engineering Products

Rubber is a unique engineering material because, unlike other engineering solids, it has high elastic deformability and an almost theoretical value for Poisson’s ratio. The stiffness of a natural rubber component in different directions may be varied independently by the judicious use of shape effects. In dynamic applications such as springs, anti-vibration mountings, bushings, and so forth, high fatigue resistance, good strength, and durability are additional points in favor of natural rubber. Natural rubber is now accepted as suitable for use in bridge bearings, in place of neoprene.

4. Latex goods

Natural rubber latex has now been largely replaced by polyurethane in foam for upholstery and bedding. The main uses of latex are in dipped goods, foam, carpet backing, thread and adhesives. Natural rubber is extremely suitable for rubber footwear manufacturing.
Important trends in rubber chemistry have taken place in every decade for the past hundred years. The future of rubber chemistry is certainly challenging but may well take on different directions.

Keeping in view, the ample potentials of radiopaque polymers, an attempt has been made in the present investigation to develop radiopaque systems from natural polymers, which are promising to be applicable in the medical field. Most of the conventional radiopaque systems are based on synthetic polymers. Radiopaque systems based on natural polymers are found scarcely. In such a scenario, owing to their excellent performance characteristics, chitosan and natural rubber were selected for present work.

1.9 SCOPE AND OBJECTIVES OF THE WORK

The work devoted to investigate the properties and applications of radiopaque polymers is meagre when compared with the volume of literature available on polymers for biomedical applications. The primary objective of the work is to impart radiopacity in selected natural polymers and to highlight their applications in medical field.

The specific objectives of the work are:

1) To select a suitable emulsion system for the preparation of chitosan microspheres and to study the effect of emulsion systems on the morphology of chitosan microspheres.

2) To introduce radiopacity in chitosan microspheres by the encapsulation of barium sulphate.

3) To prepare and characterize water soluble derivatives of chitosan like carboxy methyl chitosan, chitosan acetate and chitosan formate and to prepare radiopaque microspheres using these derivatives.
4) To prepare and characterize radiopaque natural rubber (i) by the incorporation of radiopaque fillers like zinc oxide and barium sulphate and (ii) by the iodination of natural rubber in the latex stage.

5) To study the radiopacity, physico-chemical and morphological characteristics of the polymer systems used for the investigations.

6) To prepare zinc oxide having different surface morphology using chitosan medium by an *in-situ* precipitation method and to study its effects on radiopacity in NR.
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