

Look what you can make out of silicones

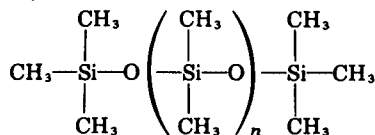
Barry Arkles

Making spare parts for the human body typifies the need for chemists to turn their attention to making "things," not just "stuff." Here I present an overview from the materials perspective of how silicones are being used in biomedical applications and illustrate with specific applications. Figure 1 suggests the range of medical uses for silicones. With them, differences in materials recommendations depend primarily on manufacturing practice and control. Modifications of mechanical or chemical characteristics of silicones generally play no a priori role in determining implantability.

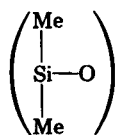
The fabrication techniques associated with medical devices include coating, bonding, extrusion, encapsulation, sealing, casting, and molding. Selection of a particular silicone is dictated both by its fabrication and performance characteristics. A single silicone material frequently is not limited to a single fabrication technique. Widely different silicones fabricated using different techniques can satisfy the same application requirements.

Some silicone chemistry

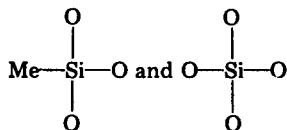
The simplest silicones are polydimethylsiloxanes (1-10). The polymers, when not cross-linked, are widely used in the manufacture of cosmetics, food-processing materials, and medicinal preparations. They are valued for their lubricity and their ability to lower surface tension and act as antifoam agents.



The repeating unit



is referred to as a D unit, while the termination unit (Me_3SiO), the trimethylsiloxy group, is referred to as an M unit. Silicones don't have to remain linear; they can have branch points:



referred to as T groups and Q groups, which introduce rigidity into the structure. This relatively simple chemistry results in fluids at low molecular weights and leads to cross-linked gums at high molecular weights. Linear, low-molecular-weight polydimethylsiloxanes are used as ingestible antifoaming agents. Under the generic name simethicone they are used to reduce heartburn and flatulence.

A variety of groups, including phenyl, vinyl, and hydrogen, can substitute for the methyl group in a silicone (Table 1). This is significant inasmuch as the substitution, branching, and molecular weight of a silicone polymer will dictate the method by which curing or cross-linking can be accomplished. Fundamentally, four processes are used to cure silicones (Figure 2). In high-temperature vulcanizing (HTV) systems, polymers containing methyl or vinyl groups are cross-linked with peroxides. In room-temperature vulcanizing (RTV) systems, two cure methods are used. In the older methods, silanols are condensed with a moisture-sensitive silane cross-linker, or a metal salt catalyzes the reaction between silicon hydrides and silanols. The latter reaction liberates hydrogen, which can be used to produce foamed products. Vinyl addition systems, in which a platinum complex catalyzes the addition of silicone hydrides to vinyl-substituted silanes, was initially used in low-temperature vulcanizing (LTV) systems but has been gradually extended to RTVs and HTVs.

The primary monomeric raw materials for silicone polymers are chlorosilanes that are corrosive, flammable, and generally difficult to handle. They are used directly or as their alkoxy derivatives only in surface treatment applications. The direct intermediates for polymers are cyclic siloxanes and low-molecular-weight silanols. The biological activity of many low-molecular-weight silanes has been established. The commonly used monomers (Figure 3) have extremely low levels of toxicity. Octamethylcyclotetrasiloxane and decamethylcyclopentasiloxane are the vehicles for "dry-feel" deodorants.

Two general methods are used to produce silicone polymers. Gums and non-silanol-terminated fluids are produced by anionic polymerization. Under typical conditions, potassium, sodium, or tetramethylammonium

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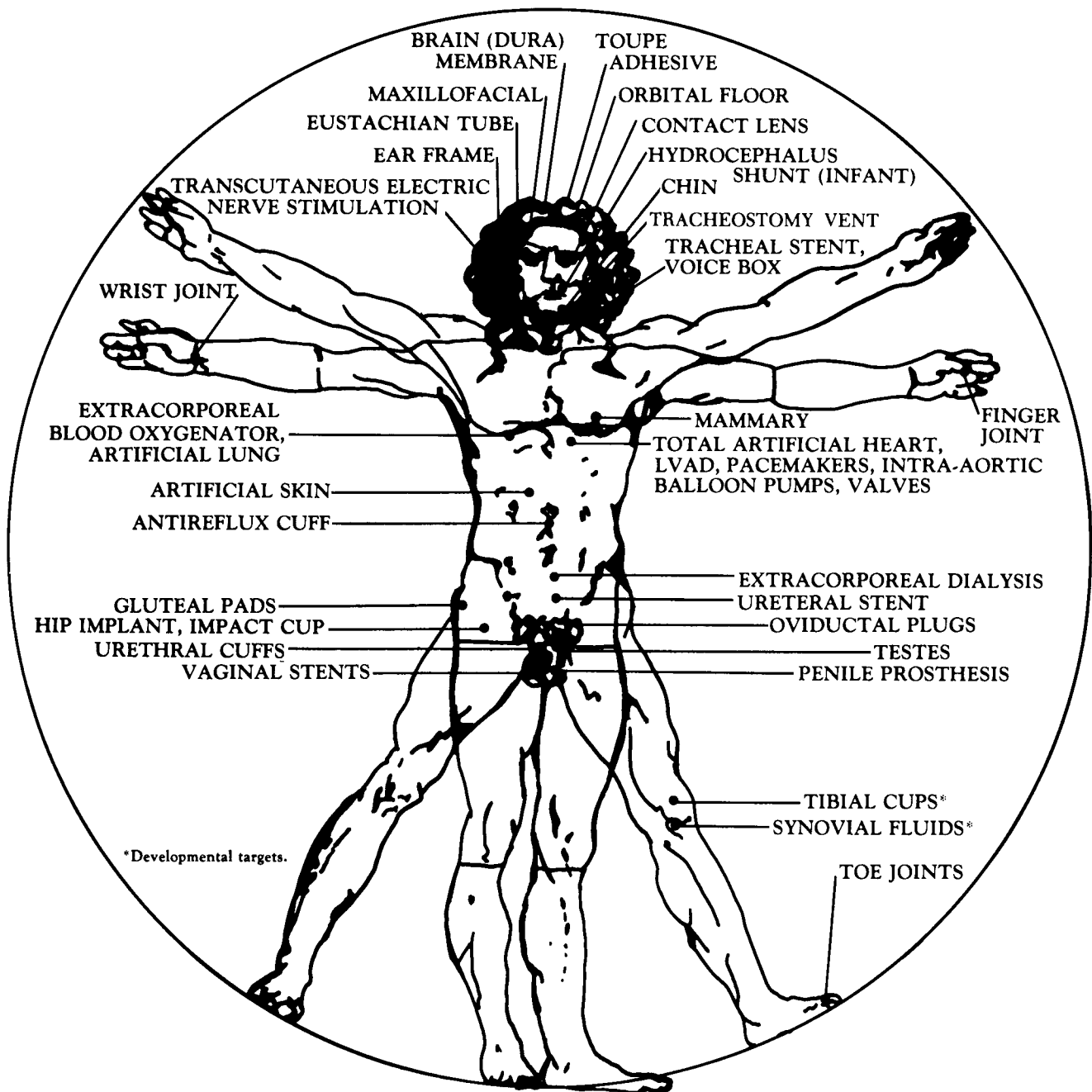


Figure 1. Silicone medical devices and the body: Numerous medical devices are made from silicone-containing polymers. Not shown are catheter and drainage devices (LVAD = left ventricular assist device)

silanolate catalysts are introduced into a mixture of monomers and end-cappers. The mixtures are equilibrated by heating under moderate conditions (60–150 °C) (11, 12). Silanol-terminated polymers are produced by a variety of techniques including hydrolysis of chlorosilanes, metal salt-catalyzed telomerization of cyclics in the presence of dimethyldichlorosilane followed by hydrolysis, and equilibration of cyclics with low-molecular-weight silanol fluids which act as chain terminators (13–15). Typical reactive silicone polymers are shown in Figure 4. They include silanol, vinyl, and hydride functional materials of various degrees of polymerization.

To increase their modulus, tensile strength, tear strength, and abrasion resistance, most silicones are filled with particulate silica. Its reinforcing effect depends on three properties: particle size, structure, and surface interaction. Particle size together with filler loading determines the area available for surface interaction. The structure determines the extent to which polymer movement is restricted under

deformation. The surface interaction determines the effectiveness with which particle size and structure control elastomer properties. Parameters associated with surface interaction include population and type of hydroxyl groups, adsorbed moisture, and chemical treatment. The redistribution of stress among polymer chains in reinforced systems is probably accomplished by two-dimensional mobility of polymer chains that are otherwise bound tightly to the silica surface.

Chemical treatment of silica may greatly change its interaction with silicone polymers. Fused silica behavior can be altered by inactivating the isolated silanol with various silanes. Materials used to modify surface characteristics include hexamethyldisilazane, divinyltetramethyldisilazane, and cyclic and short linear siloxanes. Under-treatment of silica results in “crepe hardening,” a condition in which uncured elastomer exhibits crumbling rather than plasticity under applied stress. Over-treatment of filler results in nonresponsive or “dead” elastomers. High tear strength

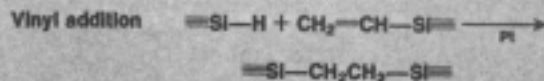
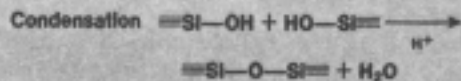
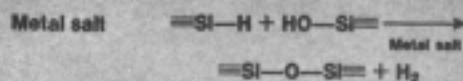
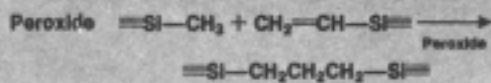
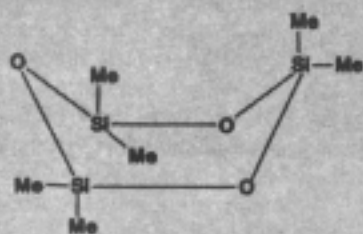
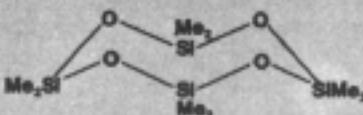


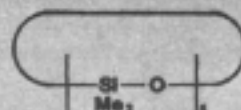
Figure 2. Silicone curing systems



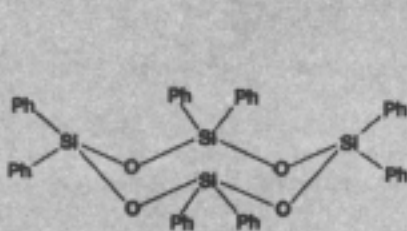
Hexamethylcyclotrisiloxane



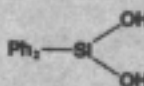
Octamethylcyclotetrasiloxane



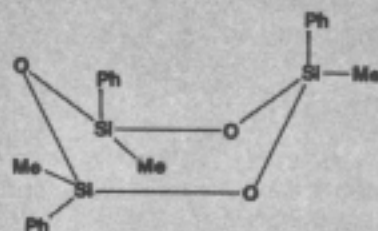
Decamethylcyclopentasiloxane



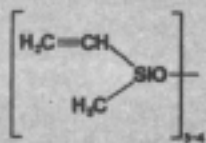
Octaphenylcyclotetrasiloxane



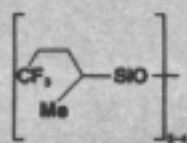
Diphenylsilanediol



Trimethyltriphenylcyclotrisiloxane



Vinylmethylcyclosiloxanes



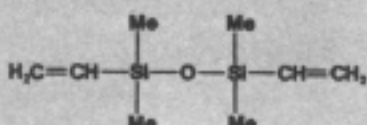
Trifluoropropylmethylcyclosiloxanes



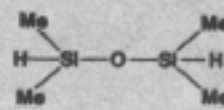
Methylhydrocyclosiloxane



Hexamethyldisiloxane



Divinyltetramethyldisiloxane



Tetramethyldisiloxane

Figure 3. Silicone monomers and terminators



Photo 2. Here actor Dustin Hoffman has aged to 121 years for the film "Little Big Man." The mask and other appliances are made of silicone and bonded by PSAs. These materials are non-sensitizing and are used in a wide range of bonding applications, including surgical dressings, ileostomy and colostomy appliances, and toupés (courtesy Dow-Corning Corp.)

Monomers and curable systems. The hydrolysis and condensation of alkoxy silanes leads to resinous products that have traditionally been used as coatings and encapsulants. In a manner consistent with this chemistry, slow-release antitumor devices have been produced by hydrolyzing the silanes in the presence of various drugs (27).

The direct polymerization of monomeric siloxanes such as hexamethylcyclotrisiloxane (D_3) and octamethyl cyclotetrasiloxane (D_4) is of current interest in the preparation of filler-free silicone rubber (FFSR). On many occasions undesirable biological responses to filled standard silicone rubber (SSR) has been attributed to the filler rather than the silicone itself. Physiological reaction to fillers is especially notable in devices with large surface areas, such as oxygenator and dialysis membranes. FFSR is more often achieved by reaction of prepolymers than polymerization of monomers.

Chawla reported plasma and radiation polymerization of D_3 for the production of filler-free silicone coatings and bulk moldings (28-31). In this method, D_3 is melted and cast or applied to a polymer substrate, then subjected to high-energy polymerization. The materials have tensile strengths of 2.5 MPa and elongation of 500%. In work with whole canine blood, cell adsorption is reduced 30-35% when compared to SSR.

Prepolymer fluids and unfilled polymers

The importance of unfilled silicone membranes in oxygenation and dialysis cannot be overemphasized. Silicone is 10 times more permeable to oxygen than natural rubber and low-density polyethylene, and 100 times greater than butyl rubber and nylon (32). For example, oxygen would diffuse at approximately 60 L/h through 1 m² of silicone 1 mL thick under a pressure of 1 atm. Man at rest consumes 18 L of oxygen/h (Photo 1).

Filler-free silicone rubber can be prepared by

cross-linking unfilled silicone gum stocks. Membranes for artificial lungs are fabricated by using 1-1.5% dichlorobenzoyl peroxide to cross-link a polydimethylsiloxane gum. The gum is cured at 100 °C for 5 min, followed by a 4-h postcure at 150 °C. In another method, a vinyl-modified dimethylsiloxane gum and peroxide are dissolved in toluene and cast into a film. After drying at 75 °C, the film is cured in air at 180 °C and subjected to UV radiation from germicidal lamps (33, 34).

Pressure-sensitive adhesives. Many of the unfilled cured silicone polymers used in medical devices can be described as pseudointerpenetrating polymer networks. The materials contain two polymer components. One silicone is a matrix material with a linear structure. The second silicone component has a branched or cross-linked structure that extends homogeneously throughout the matrix. The systems behave in a uniform, cohesive manner, although unlike true interpenetrating polymer networks (IPNs) only one component is cross-linked.

Pressure-sensitive adhesives are generally formulated from a high-viscosity silanol-terminated fluid and a low-molecular-weight resinous silicone. The two-component system is supplied in a solvent. The materials are used externally for adhering ileostomy and colostomy appliances, attaching electrodes, and adhering maxillofacial medical devices. The adhesives also have nonmedical uses (see Photo 2).

Gels. Silicone-based pseudointerpenetrating polymer networks, which result in clear, resilient gels with cohesive properties, are useful in orthopedic pads, particularly breast implants (35, 36). The gels used for orthopedic pads in breast implants (Photo 3) are generally produced by vinyl addition chemistry. The first gels used for these purposes were linear siloxanes with low levels of cross-linking (for example, a 500-700-centistoke (ctsk) dimethylsiloxane fluid with 1.0%

elastomers result from filler treatments that introduce vinyl groups.

Monomers and low-molecular-weight resins

Surface treatments and molecular coatings. Reactive monomeric and oligomeric silanes are used to impart specific surface properties to inorganic and silicone substrates. The materials have the general structure $R_{4-n}SiX_n$ where $n = 1$ to 3, and X is an alkoxy or chlorine. The electronegative group is removed by hydrolysis to form an unstable silanol which condenses with the -OH group of substrates. If there are three hydrolyzeable moieties, telomerization occurs during deposition, and coatings 6-8 molecular layers thick usually result. For details of this chemistry, see Reference 16.

Monomeric and oligomeric silanes are not sold as medical-grade materials. They are widely used in industrial products, including composites, coatings, and adhesives, to form water-repellent surfaces. It is imperative that those who use these materials for medical devices ensure that excessive monomer and hydrolysis by-products are removed after surface treatments.

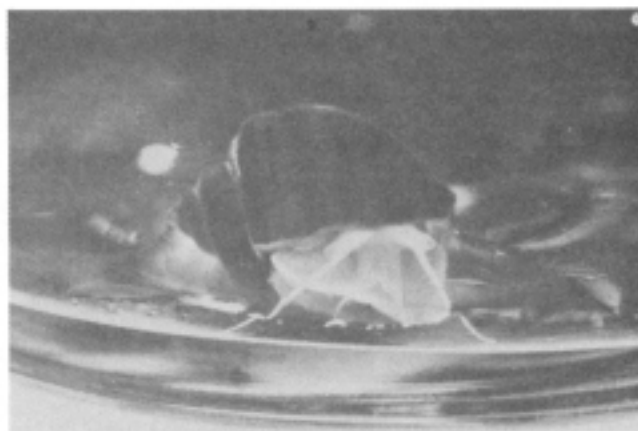


Photo 1. The low toxicity and high gas permeability of silicones are shown in this experiment, in which snails completely immersed in 3-5-ctsk polydimethylsiloxane lived for more than 72 h (author's experiment constructed from unpublished work of R. LeVier)

Silane surface treatments are employed in clinical analytical techniques to reduce interaction of blood with hydrophilic surfaces. Water-soluble derivatives of octadecylsilane are used to reduce absorption of red blood cells on glassware. Oligomeric silanes with active chlorine or alkoxy termination are not only hydrophobic, but oleophobic. Other silanes perform more active roles, enhancing adsorption or bonding of specific proteins such as heparin, bioactive groups such as fungistats, or whole cells and cell organelles. Silanes have been used to covalently bond enzymes and cofactors to inorganic substrates (Table 2).

Table 1. Silicone substitutions

Structure	Name	Application
CH_3-	Methyl	Basic substitution found in virtually all silicones; a cross-linking point with peroxide cures
C_6H_5-	Phenyl	Increases modulus, thermal, and UV stability; raises refractive index; decreases reactivity with peroxides
$CF_3CH_2CH_2-$	Trifluoropropyl	Increases stability, increases solvent resistance
$H-$	Hydride	Introduces metal-catalyzed and vinyl-addition cross-link sites
$HO-$	Silanol	Cross-linking point for condensation and metal-catalyzed cross-linking
$CH_2=CH-$	Vinyl	Increases peroxide reactivity; introduces cross-link points for vinyl addition

Table 2. Surface treatments and molecular coatings

Silane type	Application	Trade name	Reference
Octadecyl	Reduces protein adsorption	Siliclad, Glassclad 18	18, 19, 20
Chlorinated siloxane telomer	Reduces protein adsorption, reduces thrombogenicity, increases oleophobicity	Glassclad 6C, Dri-Film	20
Aminopropyl	Adsorbs heparin		17
Polyethylenimine	Adsorbs proteins	Glassclad IM	19
Octadecyl quat	Fungistatic treatment	D.C. 5700	21-23
Amine, <i>p</i> -nitrobenzamide, mercapto	Immobilization of enzymes		24, 25
Heparin	Anticoagulant	Glassclad HP	26

vinylmethyl backbone was cross-linked to 4-5 ctsk polymethylhydrosiloxane by platinum-catalyzed addition (37). In most updated formulations, vinyl-terminated siloxanes of 1000 ctsk or greater are cross-linked with a methylhydro-dimethylsiloxane copolymer using a complex of neutralized chloroplatinic acid in divinyltetramethyldisiloxane or vinylmethylcyclosiloxanes. However, this cross-linked system constitutes only 10-20% of the gel weight; the matrix material is 350-1000 ctsk polydimethylsiloxane. The cross-linked silicone produces an interpenetrating polymer network within the matrix silicone, which creates a responsive gel with good cohesion (38-41). Another approach to gel formation is to produce a hydrophilic copolymer between a vinylsiloxane with hydrolyzable groups and vinylpyrrolidone (42, 43).

An undesirable property of pseudointerpenetrating silicone networks is for a small portion of the matrix polymer to bleed out. The matrix material can bleed through fully cross-linked polydimethylsiloxane mammary shells. Bleeding can be reduced by coating or preparing shells from

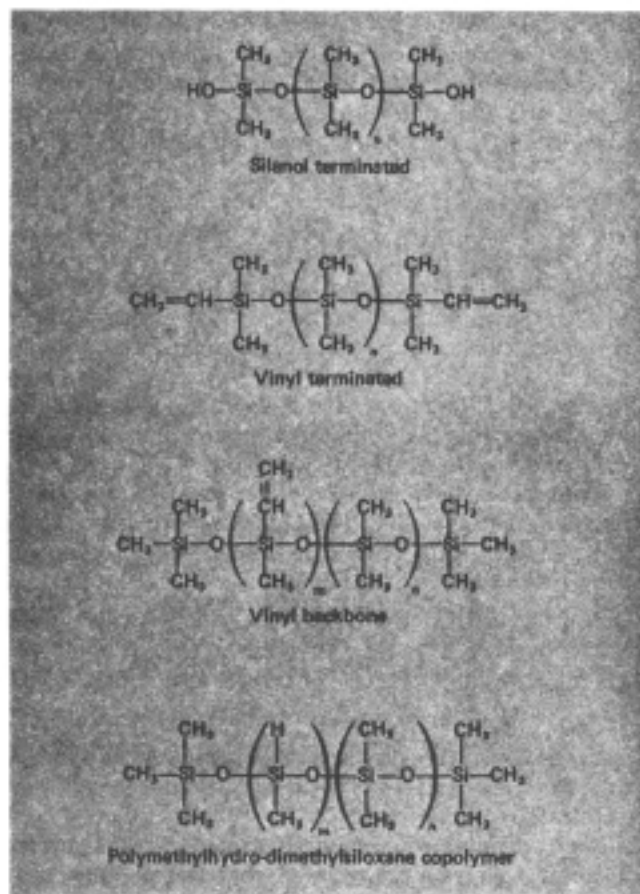


Figure 4. Silicone polymers



Photo 3. Reconstruction of the breast following mastectomy is accomplished with a mammary prosthesis fabricated from a silicone-membrane-encapsulated silicone gel (courtesy W. Lynch, N. Georgiade)

phenyl- or trifluoropropyl-containing siloxanes (44). The different solubility parameters for these materials allow them to behave as barriers for polydimethylsiloxanes.

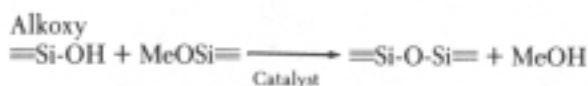
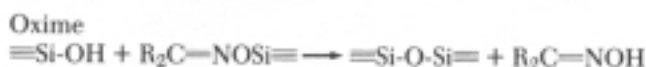
Elastomers

The most widely recognized silicones are filled or reinforced elastomeric products. The two main classifications of materials are: low consistency (not requiring simultaneous application of heat and pressure for processing) and high consistency (requiring simultaneous application of heat and pressure). All of the cure systems mentioned earlier are used in the elastomeric products. Because there are so many products, I can only select the most representative examples here.

Adhesives and sealants. Silicone adhesives and sealants are low-consistency, room-temperature-vulcanizing liquid rubbers that offer considerable latitude in formulation and properties. The main components of condensation cure room-temperature-vulcanizing systems (RTVs) are silanol-terminated polydimethylsiloxanes. The viscosity of the polymer can range from 500 to 1 million ctsk. Often a blend of polymers will be used in compounding. This allows

variations in cross-link density, cure times, and working consistencies.

Most RTVs of this class have moisture-sensitive cure systems. They contain a silane cross-linker with moisture-sensitive hydrolyzable groups. The most common systems are:



Reactions of these systems are often catalyzed with carboxylic acid salts of tin, zinc, iron, or titanium. Tin octoate is a fast catalyst; dibutyltin dilaurate is a slow one. In general, amines and oximes react fastest, followed by acyloxy, then alkoxy. Excess silane gives slower reacting materials with longer pot-life. It is best to adjust cure times during compounding.

To choose a material for a particular application, one must consider physical properties and processing. One-part RTVs tend to be used as adhesives. Two-part RTVs tend to be used as sealants and encapsulants. Either type can usually be dispersed in solvents as required for processing.

An important application for low-modulus silicones that derive from condensation-cure silicone adhesives is the fabrication of biodegradable templates to close deep wounds or cover third-degree burns. Artificial skin (45-47) is a bilayer of membrane fabricated from a cross-linked mixture of bovine hide, collagen, and chondroitin 6-sulfate derived from shark cartilage, with a 0.5-0.8-mm cured top layer of silicone (Figure 5). The artificial skin serves during both the traumatic and regenerative stages of skin tissue damage. The bilayer membrane seals the wound, preventing fluid loss and proliferation of bacteria. The collagen-chondroitin layer behaves as a regenerative template for new tissue growth, by seeding the membrane with cells that synthesize new skin tissue. During the regenerative process the silicone membrane provides a pliable mechanical support and allows moisture transmission. In the final stages of new skin growth, the collagen-chondroitin layer is physiologically degraded and the silicone layer is nontraumatically ejected.

Silicones provide a novel approach to birth control. A low-consistency RTV silicone that cures to a low-modulus silicone after catalysis with stannous octoate is injected into the fallopian tubes (Photo 4, Figure 6) (48-50). The silicone forms a mechanical plug, blocking travel of the ovum to the

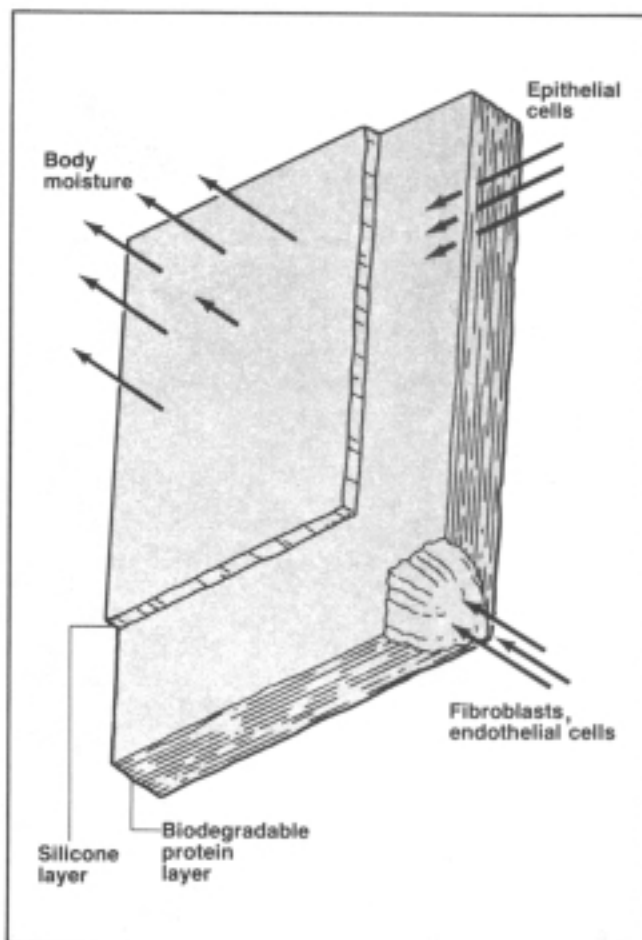


Figure 5. Artificial skin makes use of silicone as a moisture- and oxygen-permeable mechanical support and barrier for a polymer derived from shark cartilage, which acts as a template for skin formation (from Yannas)

uterus. The silicone conforms to the tubal lumen before vulcanization and remains flexible afterwards. Incorporation of a retrieval ring at the uteral end of the plug makes the procedure readily reversible. This device is in the later stages of clinical trials. More than 1000 volunteers now have the silicone plugs in place.

A harbinger of an entire generation of drug administration devices is the collection of continuous drug delivery devices developed by Alza Corporation (51, 52). In these applications the drug is dispersed and cured in a silicone, with which it has poor compatibility. The silicone drug reservoir is encapsulated by a polymer which is permeable to the drug. A Fick's law relationship can be established for each drug-membrane system and by adjustment of parameters, a device with a predetermined rate of drug delivery consistent with pharmacological requirements can be produced. In contraceptive applications, an intrauterine device releases progesterone at a constant rate. Because administration is local rather than systemic, side effects and total dosage are reduced. Other applications for constant drug delivery include pilocarpine for glaucoma and scopolamine for motion sickness. In this case a backed-delivery system is affixed to the skin and the drug is delivered through it.

Low-consistency elastomer—addition cure. Addition cure materials tend to have greater strength than condensation cure products. They are thought of as clean systems since there are no by-products or hydrolyzable leaving groups during cure. Cure rate may be adjusted from

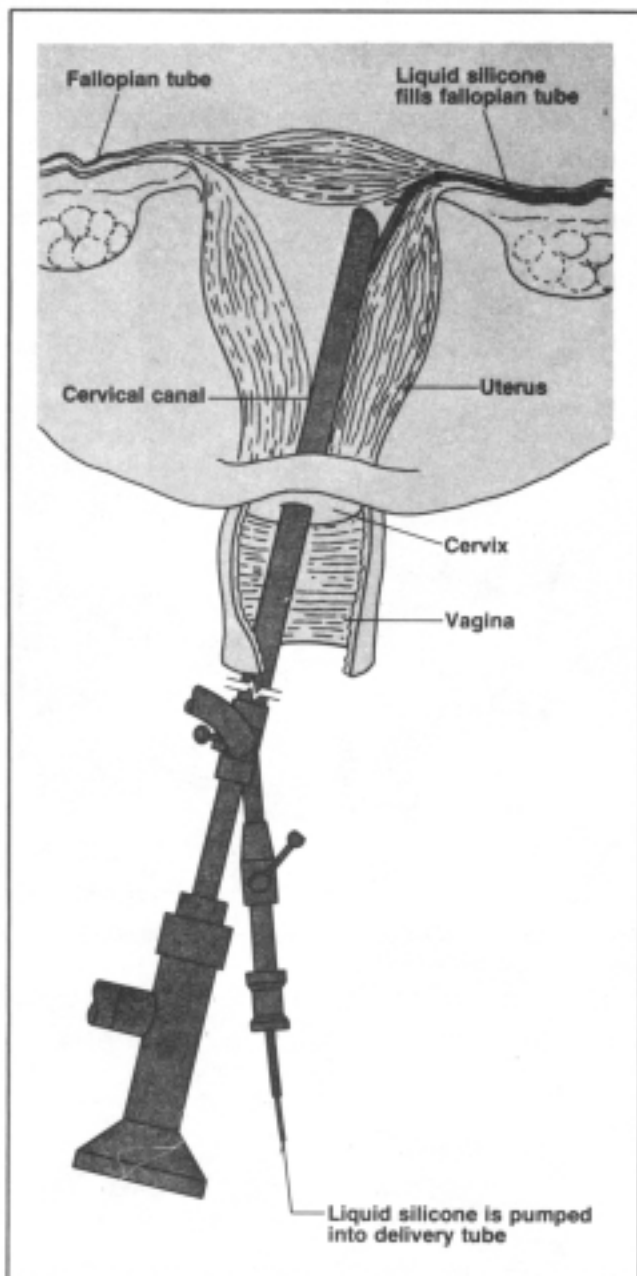


Figure 6. A tin-catalyzed silicone RTV is injected into the fallopian tubes, where it polymerizes to form a plug. The contraceptive method is reversible

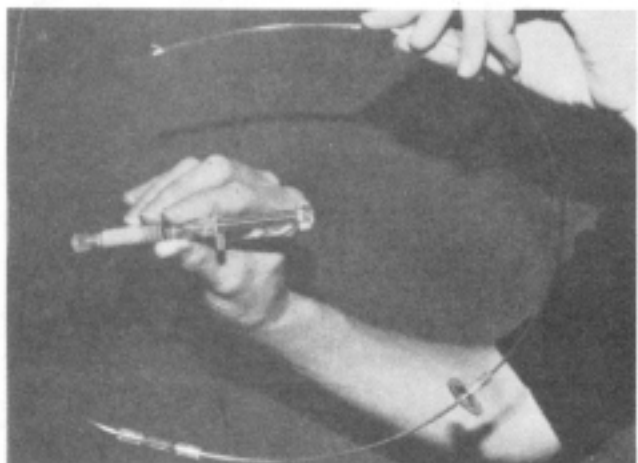


Photo 4. The device used to implant the oviductal plugs (courtesy R. Erb, Franklin Research)

minutes to hours depending upon the use of inhibitors or level of catalyst.

The viscosity may vary from 1000 to 1 million ctsk. Lower molecular weight polymers are used to formulate dental impression materials (48-53), while higher molecular weights are used in liquid injection-molding compounds.

Addition cure materials are supplied as two-part systems. Generally the catalyst, a platinum complex, is in part A and the cross-linker, a hydride, is in part B. Cross-link density may be adjusted by the distribution of hydride along the siloxane chain and length of the chain. Short chains with high hydride give material with a more resilient character and are used in formulating products with high tensile and tear strengths. Longer chains with lower hydride content give greater elongations. Typical Pt levels in these formulations range from 5 to 75 ppm. Inhibitors may be used to moderate the rate of cure. They differ from "poisons" in that their interaction with the platinum complex is reversible. Poisons include sulfides and sulfur-containing rubbers and certain amines.

Few of the addition cure systems are sold specifically as medical-grade materials. One such material, which is used for biomedical encapsulating and moldmaking, is Dow Corning's MDX-4-4210 (54). Typical properties are given below:

- viscosity, as supplied, 80 000 ctsk
- durometer, >25 shore A
- tensile strength, >3.8 MPa
- elongation, >350%
- specific gravity, 1.12.

Low-consistency elastomers are also important in maxillofacial applications. Loss of facial sections are usually due to trauma or skin cancer. The psychological devastation of the massively disfigured individual and the disruption of normal social relations emphasize the importance of these prostheses. Silicones in this application must be plastic in the artistic sense, readily pigmentable with reflective properties similar to those of skin. Traditionally, polydimethylsiloxane clean-grade elastomers have been used. Newer grades that have phenylethyl side chains or other groups that enhance pigmentability are under development. Transcutaneous nerve stimulators are fabricated from conductive silicone. They are used for treatment of chronic severe pain by administering low-level voltage to underlying nerves, preventing transmission of pain impulses to the brain. Introduction of highly conductive materials such as carbon and silver into both low- and high-consistency silicones allows electrodes to be fabricated from these materials.

High-consistency elastomers. The oldest and most widely used silicones are the peroxide cure high-temperature vulcanizing (HTV) systems (Table 3) (2). They are used for extrusion of catheter tubing, compression molding of shunts and flexing joints (55), and calendaring sheeting, both

Table 3. Typical properties of high-consistency silicone

Property	Measurement
Specific gravity	1.12–1.25
Durometer, shore A	25–75
Tensile strength, MPa	5.9–8.3
Elongation, %	350–700
Tear strength, kN/m	12–28
Compression set 24 h at 175 °C (%)	10–40
Dielectric constant	2.8–2.9
Dissipation factor	$6.0\text{--}9.0 \times 10^{-4}$

Dacron-reinforced and nonreinforced. Uncured forms can be fabricated by manual or "lay-up" techniques.

An excellent example of medical device technology that incorporates a wide range of filled silicone elastomers is penile prosthesis for certain individuals with nonpsychogenic impotence. In the Finney-designed flexible rod prosthesis, four different biocompatible silicones are used (56). A soft silicone encapsulates a semi-rigid rod. A pair of devices is implanted in the corpus cavernosi of the penis—the tissue that normally becomes engorged with blood during erection. Once implanted, the individual can manually elevate the penis. An even more complex design is the inflatable penile prosthesis, which is designed to mimic natural erection (57) (Photo 5, Figure 7). Inflatable cylinders are implanted in the corpus cavernosi, a pumping bulb is incorporated in the scrotum, and a reservoir is incorporated into the peritoneum. By use of a simple hydraulic system the cylinders may be inflated to elevate the penis or released to relax the penis. A wide range of silicone elastomers are used to fabricate the cylinders, pumps, tubing, and balloon reservoirs.

Thermoplastic silicones

Thermoplastic silicones include silicone copolymers, block copolymers, IPNs and some alloys. A substantial portion of the polymer composition does not contain a siloxane backbone. These materials differ radically from conventional silicones. Mechanical strengths are higher, but a variety of other striking property differences are also introduced.

Silicone-urethanes. The mechanical, fatigue, and physiological response characteristics of silicone homopolymers are not comparable to those of silicone-urethanes used in blood pumps, intra-aortic balloons, total heart replacements, and related devices (Table 4, Photos 6 and 7) (58). Fatigue strength, toughness, flexibility, and low interaction with plasma proteins are bio-engineering criteria applicable to silicone-urethanes. The most widely recognized material in this category is Cardiothane 51 (formerly Avcothane 51) produced by Kontron Cardiovascular, Inc. The material is described as

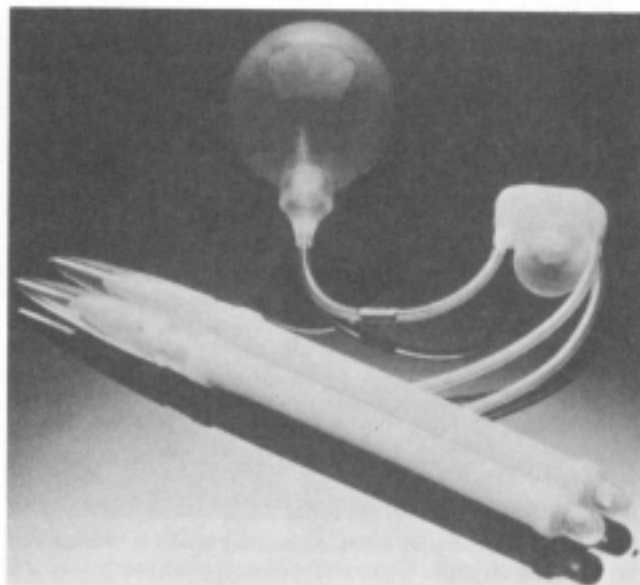


Photo 5. The penile prosthesis (courtesy J. Giantz, American Medical Systems)

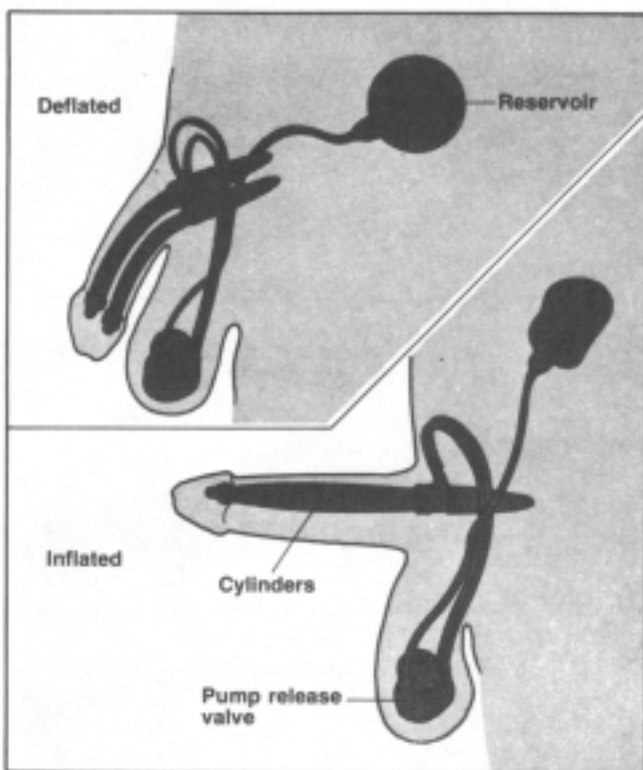


Figure 7. The inflatable penile prosthesis is used to correct certain forms of nonpsychogenic impotence. Inflatable cylinders are placed in the corpus cavernosi of the penis, and an inflation pump with relief valve is placed in the scrotum. A reservoir is placed in the peritoneum (courtesy American Medical Systems)

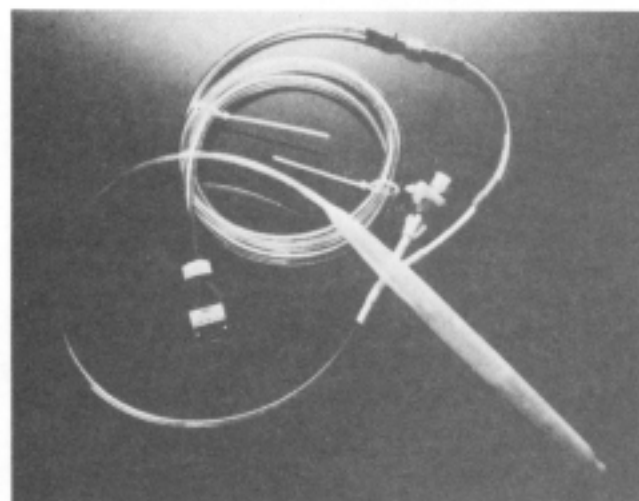


Photo 6. Intra-aortic balloon pumps, requiring mechanical and fatigue strength along with physiological inertness, are fabricated from silicone-urethanes (courtesy Kontron Cardiovascular)

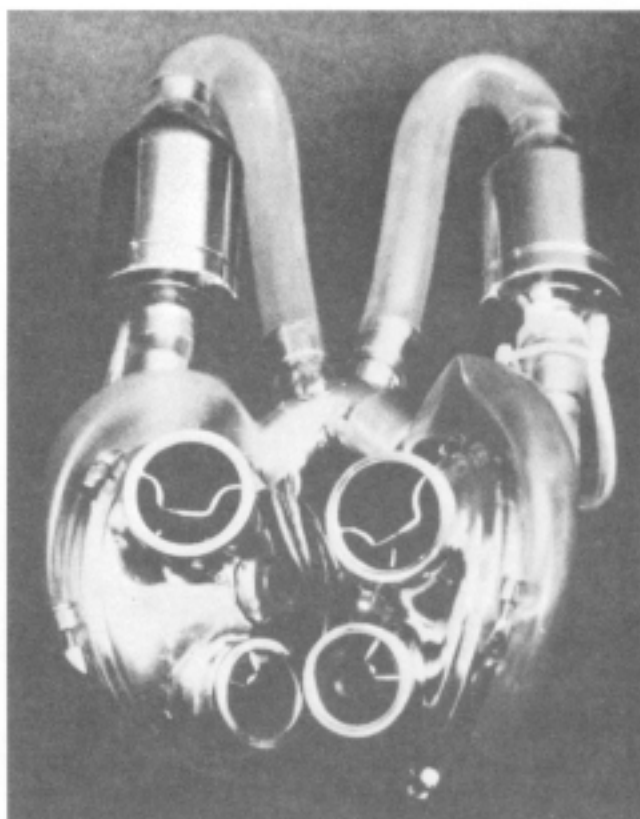


Photo 7. This artificial heart, a totally implantable, hydraulically driven total cardiac prosthesis, is constructed with silicone-urethanes (courtesy R. Ward, Thoratec Laboratories)

Table 4. Silicone-urethane mechanical properties

Description	Cardiothane 51	PTUE 102
Manufacturer	Kontron	Petrarch
Processing	Dipping, casting	Molding, extrusion
Silicone, %	10	10
Specific gravity	.95	1.00
Tensile strength, MPa	43.8	41.4
Elongation, %	525	450
Tear strength, kN/m	86	130
Water absorption, 24 h	1.6%	.03%
Hardness, shore	A72	D50

a copolymer of aromatic polyether urethane and polydimethyl-siloxane (59). The copolymer is proposed to cross-link by the interaction of acetoxy-terminated siloxane blocks with substituted urethane nitrogens (60). The polymer is not homogeneous and may be described as a mixture of 10% moisture-cured polydimethylsiloxane in a urethane matrix, with bulk-phase separation prevented by small amounts of silicone-urethane surfactant formed during cure (61). Cardiothane is primarily a casting resin. Molding and extrusion grades of silicone-aromatic polyester urethanes IPNs are available from Petrarch Systems (Table 4, Photo 8).

While not yet commercially available, several true urethane-siloxane copolymers with promising properties are in development. One approach is to use a carbinol (C-OH) transition between the siloxane and urethane (62-64). A carbinol-terminated silicone can be created by reacting silanol-terminated polymers with ethylene oxide to yield a hydroxyethyl ether ($\text{SiOCH}_2\text{CH}_2\text{OH}$), and by adding allylic alcohols to hydride-terminated polymers to produce materials with greater hydrolytic stability ($\text{SiCH}_2\text{CH}_2\text{CH}_2\text{OH}$). A second approach is to use a urea transition between the siloxane and urethane which results from an aminoalkyl-terminated siloxane (65).

Silicone-polycarbonates. Silicone-polycarbonates can be injection molded and extruded. Perhaps their most unique process characteristic is their ability to be cast into films from solutions in methylene chloride or trichloropropane by dropping the solutions onto warm water and allowing the solvent to evaporate. The mechanical properties of these materials are far greater than unfilled silicones. Here are properties of silicone-polycarbonate 50:50 block copolymers:

- specific gravity, 1.07-1.08
- tensile strength, 19.0-22.0 MPa
- elongation, 270-350%
- water vapor transmission, 16-20 g/24 h · 100 m²/mL

The earliest silicone-polycarbonates were produced by condensing preformed silicone blocks with bisphenol A by phosgenation in the presence of amine (66-69). Later syntheses of these materials improved reproducibility and properties of these materials by using polycarbonate prepolymers and amine-terminated siloxane blocks (70). The physical characteristics of these materials have been

Table 5. Properties of Rimplast silicone-thermoplastic IPNs

Property	Aliphatic urethane	Nylon 12	Nylon 6/6	SEBS
Tensile strength, MPa	34.5	35.9	69.6	8.3
Elongation, %	350	20	5	1200
Flexural strength, MPa	—	55	96.5	400
Flexural modulus, MPa	—	1380	2482	3.5 at 300%
Tear strength, kN/m	>60	—	—	25

extremely well defined (71, 72). Silicone-polycarbonates have high mechanical and tear strengths, while maintaining a high degree of oxygen and water permeability.

Blood oxygenation, dialysis, and microelectrode membranes are the usual biomedical applications for silicone-polycarbonates. The simple unmodified materials are used in blood oxygenation (73). Techniques for preparing thin, high-temperature membranes for oxygen transport have been described previously (74-76). Silicone-polycarbonates have been cast as defect-free membranes 0.015 μ thick.

In microelectrode applications, these simple block polymers have inadequate hydrolytic stability and their dielectric constants are too low to permit ion transport. Thus many current microelectrode materials incorporate ion-carrier groups in the siloxane block to allow molecular transport as well as a urethane transition to the polycarbonate to increase hydrolytic stability (77-80). The combination of mechanical, dielectric, permeation, and film formation properties has allowed the preparation of membranes useful for monitoring physiological changes in concentrations of hydrogen, potassium, sodium, and ammonium ions (69, 70). A typical structure is shown in Figure 8.

Silicone-methacrylates, ophthalmic materials. Once it was recognized that maximum contact lens comfort was achieved when the eye could "breathe," silicones became likely candidates for lens materials (Photo 9). The primary design parameters that lead to selection of silicone materials are permeability (Dk) and equivalent oxygen percentage (EOP), a finished lens measurement that considers oxygen demand of ocular tissue. Other parameters requiring modification of basic silicone properties are wettability (contact angle), dimensional stability, and refractive index.

A minimum EOP of 5-7% has been proposed for finished lenses (81, 82). This is equivalent to the oxygen available to the eye during sleep (when the eyelid covers the eye). An

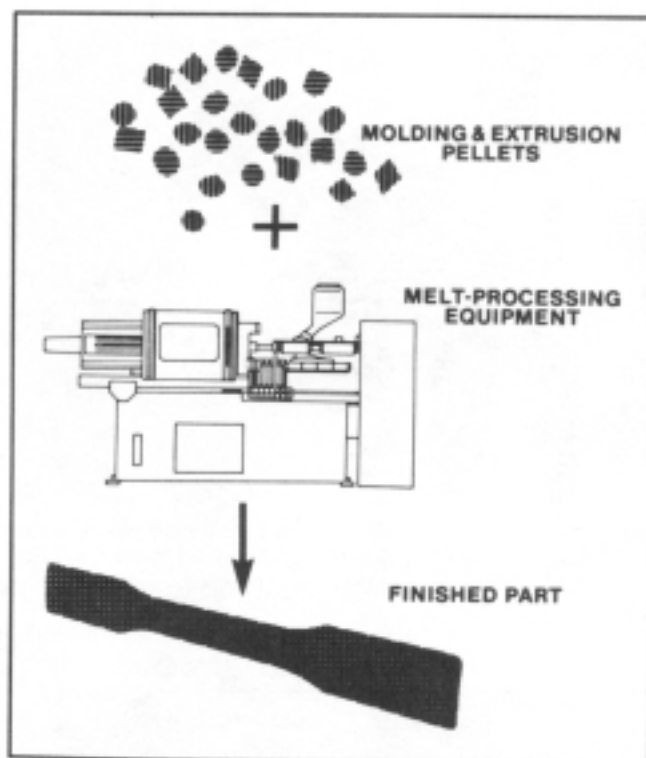


Photo 8. Rimplast process for silicone-thermoplastic IPNs makes use of a homogenous two-component blend of thermoplastic pellets which react under melt conditions to give a silicone IPN product (Petrarch Systems)



Photo 10. Catheter tubing extruded from Rimplast silicone-urethane and silicone-nylon 12 systems exhibits greater mechanical strength and tear resistance than traditional silicones while maintaining physiological inertness (Petrarch Systems)



Photo 9. Hard oxygen-permeable contact lenses allow correction of a wider range of visual defects without compromising wearer comfort (courtesy R. Capozza, Syntex Ophthalmics)

EOP below 2 causes corneal edema. Figure 9 shows how the EOP relates to permeability for various lens thicknesses and various lens materials.

Trends in the early 1970s toward soft lenses bolstered interest in pure siloxane backbone materials which have the highest Dks. A variety of mechanical, optical, and wetting problems posed a considerable challenge. No siloxane backbone lenses have achieved commercial acceptance. A recently introduced lens that incorporates siloxane backbone technology is offered by Dow Corning as Silsoft. A newer approach is to use siloxane-modified methacrylate copolymers. This polymer technology leads primarily to hard lenses and is now an established commercial technology. The most conspicuous example is the Polycan Silofocon lens offered by Syntex.

The enhancement of oxygen permeability in siloxane lens

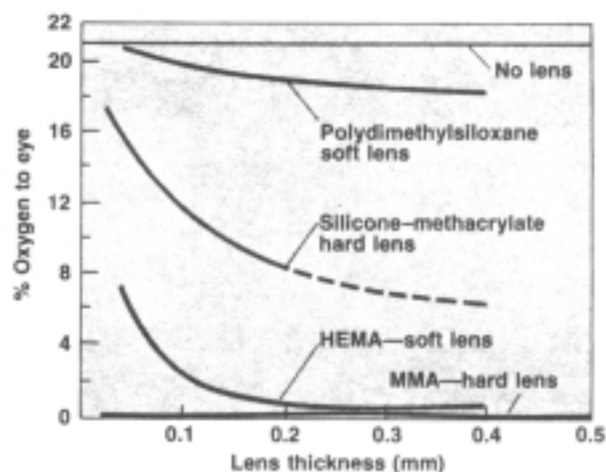


Figure 9. Oxygen permeability of contact lenses (from Hill)

systems is associated with high relative proportions of silicon-oxygen and silicon-carbon bonds. These long bonds lead to a free volume element which in the case of polydimethylsiloxane is 5-6 times greater than that of polymethacrylates (83). Both polydimethylsiloxane and polyvinyltrimethylsilane exhibit high oxygen permeability when introduced into copolymer systems. It appears that a maximum disordering of polymer structure (i.e., random copolymers or terpolymers) is desirable. Polymers should be designed to exclude microblock regions that are large enough to phase separate. In order to provide satisfactory dimensional stability the systems are cross-linked.

The earliest silicone lens materials were dimethylphenylmethyl-siloxane copolymers containing sufficient phenyl groups (10-15 mol %) to match the refractive index of the polymer- to silica-reinforcing fillers. These were peroxide cure elastomer systems (84-86). Lenses based on this chemistry were extremely hydrophobic, causing discomfort and in many instances damage to the cornea. Water permeated through the lenses from the surface of the eye. Since these unmodified siloxanes are extremely hydrophobic, water is unable to return to the tissue under the lens and dehydration of tissues along with adhesion of the lens takes place (87).

Approaches to improving the hydrophilic properties of siloxane backbone lenses have included both plasma and radiation treatment (88-90). Siloxane polymers can also be blended or grafted with hydrophilic polymer systems such as vinylpyrrolidone and glycidyl methacrylate (91-94). Surface siloxane bonds have been hydrolyzed by titanates (95).

Probably the most significant new technology in silicone hard lens materials is that disclosed by Gaylord for the production of siloxane-modified methacrylate copolymers

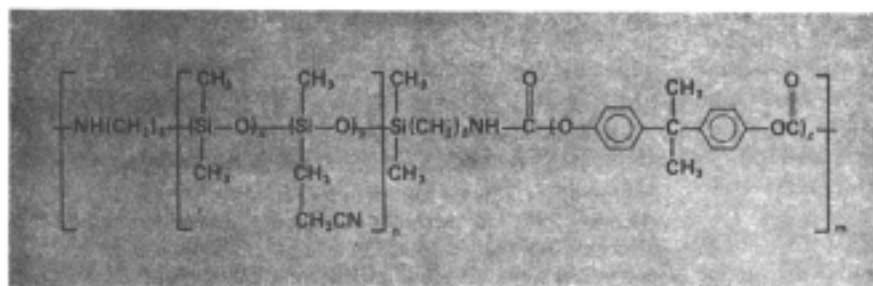


Figure 8. Block copolymer of bisphenol A polycarbonate modified for increased ion transport and hydrolytic stability

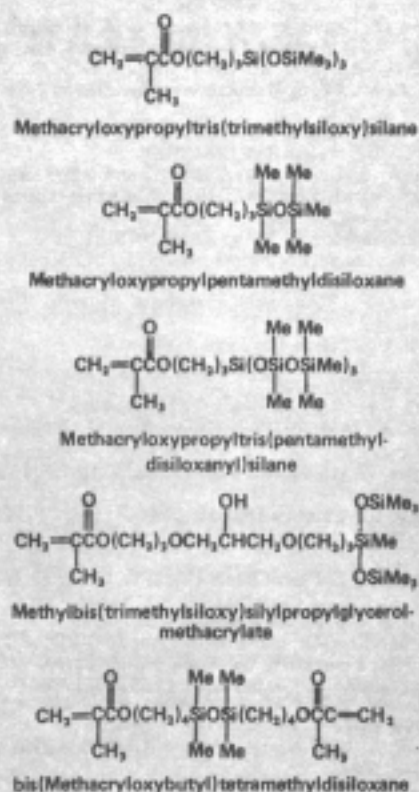


Figure 10. Contact lenses with high oxygen permeability are fabricated from monomers containing substituted siloxy pendant groups

(96-98). In the simplest example, methacryloxypropyltris(trimethylsiloxy)silane is copolymerized with other methacrylate monomers, by which means the oxygen permeability of siloxanes is combined with the mechanical and optical properties of the methacrylates. This technology is the basis of the Syntex Polycon lens, which is said to use a methacryloxypropyltris(pentamethyldisiloxanyl) silane (99). Several research groups have found other siloxane-modified methacrylates not described in the Gaylord patent (99-104). Toyo Contact Lens, for example, has prepared siloxane-modified hydroxyethylmethacrylate monomers that have pendant hydroxyl groups, which suggest improved hydrophilicity (102). This chemistry has also been translated to soft contact lens systems (103).

Other siloxane-modified methacrylate technology which appears to have considerable obstacles for commercialization is that of Bausch and Lomb, in which a bis(methacryloxybutyl) end-blocking unit is prepared and then polymerized with D_4 (104-107). This long, oxygen-permeable group acts as a difunctional cross-linking unit in the polymerization of a variety of monomers. The result is a soft lens system that is both oxygen permeable and hydrophilic. An analogous result with a different technology, reported by Ciba-Geigy, uses a urethane bridge from a polysiloxane to hydroxyethylmethacrylate (Figure 10) (63).

While not currently directed toward contact lens

formulations, silicone-acrylate copolymers develop properties that suggest future evaluation (108-110). Hard contact lenses have been produced by application of high phenyl content silicone casting resin technology (111). It also should not be surprising to see some of the silicone-polycarbonate and other oxygen-permeable membrane technologies translated to contact lens materials.

Other silicone-thermoplastic systems. A variety of other thermoplastic-silicone systems have been reported, including silicone-methylstyrene block copolymers (112, 113) and silicone-polypeptide block copolymers (114). A general technology for producing IPNs that may be applied both to engineering thermoplastics and thermoplastic elastomers has recently been disclosed (115). In this method, separate extrusions of a vinyl functional siloxane and a hydride functional siloxane with a base resin are prepared. The materials are pelletized and mixed together with a platinum complex catalyst. During molding or extrusion of fabricated parts the system is homogenized and the crosslinking is activated. The result is a silicone IPN with hybrid properties—the mechanical properties on the thermoplastic reduced blood-polymer interaction and increased oxygen and moisture permeability. Applications include catheters and load-bearing prosthetic devices (Table 5, Photo 10).

Summary

Silicones continue to be a fertile area for the development of specialty polymers. As medical device applications develop, specialty silicones are apt to develop with them. This review only provides an indication of the complexities of physiological interaction or other material alternatives that are used in implants. For an excellent review from the physiological viewpoint, see Van Noort and Black, (116), and for one from the perspective of devices see Lynch (117).

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