Lakehead University

Hydrolysis of Silicone Polymers in Aqueous Systems

by

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A Thesis

Submitted to the Faculty of Graduate Studies

In Partial Fulfilment of the Requirements for the

Degree of Masters of Science

Department of Chemistry

Thunder Bay, Ontario

Abstract

Silicon-29 and ^{1}H NMR spectroscopy were used to investigate the hydrolysis of methyl silicones in a variety of aqueous environments. Dilute acid, dilute base and one or more of the dissolved constituents of blood plasma were found to catalyse the degradation of polydimethylsiloxane (PDMS)–and its hydroxy- and methoxy-terminated derivatives–along with the interior and shell of a silicone mammary prosthesis. Dimethylsilanediol (DMSD) was the principal hydrolysis product, although in many instances (most notably after long decomposition periods) the dimer (tetramethyldisiloxanediol) and/or certain cyclodimethylsiloxane species were also detected. Only for hexamethyldisiloxane was silicic acid detected as an additional hydrolysis product after long-term interaction with blood plasma. Alcohols and certain aliphatic polyols, when added to solution, typically caused alkoxylation of DMSD and the dimer.

The presence of electron withdrawing hydroxy and methoxy end groups greatly increased the rate of degradation of PDMS. Both the shell and interior of the mammary prosthesis also hydrolysed faster than pure PDMS, which would suggest that there is considerably less than 100% trimethylsilyl capping of their constituent polymer chains.

Acknowledgments

I would like to express my gratitude to Dr. Stephen D. Kinrade for his guidance during the course of this research. I also wish to thank the members of the Prairie Regional NMR Facility (Winnipeg) for obtaining many of the NMR spectra, Dr. Christopher Knight for his assistance with NMR techniques, and members of the Lakehead University Instrumentation Laboratory for NMR training and providing the inductively coupled plasma (ICP) and mass spectrometry (MS) data. In addition, I would like to thank all past and present members of the Kinrade research group with whom I have had the pleasure of working.

I would also like to express my gratitude to Dr. Thomas Swaddle for reviewing this manuscript.

Contents

Symbols and Abbreviations

Abbreviations

cSt	centistoke
D_3	hexamethylcyclotrisiloxane
D_4	octamethylcyclotetrasiloxane
D_5	decamethylcyclopentasiloxane
DEPT	distortionless enhancement by polarization transfer
DDW	deionized distilled water (type I)
DMSD	dimethylsilanediol
DMDMS	dimethoxydimethylsilane
HMDS	hexamethyldisiloxane
HPDMS	hydroxy terminated polydimethylsiloxane
LDPE	low density polyethylene
MPDMS	methoxy terminated polydimethylsiloxane
Na-Gluc	sodium gluconate
Na-Tart	sodium tartrate dihydrate
NOE	nuclear Overhauser effect
NMR	nuclear magnetic resonance

PDMS	polydimethylsiloxane
ppm	parts per million
TES	triethyl silanol
TMDSD	tetramethyldisiloxanediol

Symbols

D_1	delay between successive NMR acquisition sequences
δ	NMR chemical shift (ppm)
H	hexaoxo- coordinated silicon
J	nuclear spin-spin coupling constant
K	equilibrium constant
P	pentaoxo- coordinated silicon
Q^x_y	tetrahedral SiO_4 centre, x indicates number of siloxane linkages, y indicates the number of equivalent centres in a symmetrical species
T_1	spin-lattice relaxation time
T_2	spin-spin relaxation time

Chapter 1-Introduction

Silicon Biochemistry

Silicon is the second most abundant element in the Earth's crust and is ubiquitous (10^{-5}-10^{2} ppm) in the hydrosphere. Consequently, it is readily accessible to biological systems [1]. Indeed, some plants cannot survive without silicon while many others require it to defend against physical and biological stresses [2]. However, very little is known about how silicon is utilized by plant life. In addition, research has demonstrated that silicon is required as a trace element for the healthy development of bone and cartilage in animals [3-7]. It has been postulated that organic hydroxyl groups, such as those present in saccharides and catechol derivatives, condense with silanol groups and thereby play an important role in the transport, uptake and possible utilization of silicon [8].

Despite the apparent need for silicon in biological systems there has been no evidence so far of Si-C or Si-O-C bonds forming in nature, which has led some workers to question the very existence of silicon biochemistry [3, 9]. However, in 1999 Kinrade *et al.*[10] showed that stable, alkoxy-substituted alkaline anions form when aliphatic mono or polyhydroxyl alcohols are added to a sodium silicate solution. Moreover, certain aliphatic polyhydroxyl alcohols yield polyolato silicate complexes containing either pentaoxo or hexaoxo silicon centred complexes (represented as P and H respectively) [11], even at circum neutral pH's [12]. Recently, the first ever silicic

acid transporter protein was identified [13]. These proteins contain hydroxyl rich regions which condense with silicate species, possibly facilitating the active biotransport of silicon [14a, 14b]. Hydroxyl groups are also known to affect the rate of condensation of silicic acid [15] giving additional evidence that organic hydroxyl groups play an important role in bio-silicification.

Silicone Polymers

Silicone is a general term for organosiloxane polymers containing a backbone of tetrahedral silicon and bridging oxygens. In the most common silicone polymer, polydimethylsiloxane (PDMS), the remaining Si coordination sites are occupied by methyl groups.

In industry, silicones are made based on a method developed by Eugene Rochow in 1940. In this method, a stream of methyl chloride and hydrogen chloride gas is passed over a bed of silicon containing a copper metal catalyst. Two moles of methyl chloride react with one mole of silicon to form dichlorodimethylsilane. When dichlorodimethylsilane is combined with water, hydrochloric acid and, initially, dimethylsilanediol (DMSD) are formed [16]. Dimethylsilanediol is highly susceptible to condensation polymerization reactions, resulting in two key intermediates in the production of siloxane polymers [17], cyclic dimethylsiloxanols and linear polydisiloxanols. Cyclic dimethylsiloxanols undergo ring opening reactions to form linear siloxanols, which can then undergo condensation reactions to form higher molecular weight polymers.

Silicones are typically represented using "M, D, T, Q" shorthand notation which denotes the number of coordinated oxygens at a given tetrahedral Si centre. M represents a silicon coordinated to one oxygen, while D, T, and Q centres are linked to two, three and four oxygens, respectively. See Figure 1.1. The molecular weight, branching, and shape of the polymer is controlled by changing the relative proportions of the M, D, T and Q units.

PDMS, accordingly represented as MD_nM, is the most commonly used silicone polymer due to its excellent chemical, thermal and photo stability. In addition, its physical and dielectric properties remain constant over a wide range of temperatures [17]. Low molecular weight PDMS is typically used for lubricants, water repellents, anti-foam agents and cosmetics. Moderately high molecular weight PDMS polymers are used in high temperature hydraulic and heat transfer applications. In addition, the medical industry uses high molecular weight PDMS for reconstructive surgical implants, cardiac pacing devices, toe and finger joints, and catheters [18].

Even with their apparent inertness, silicone polymers will depolymerize under

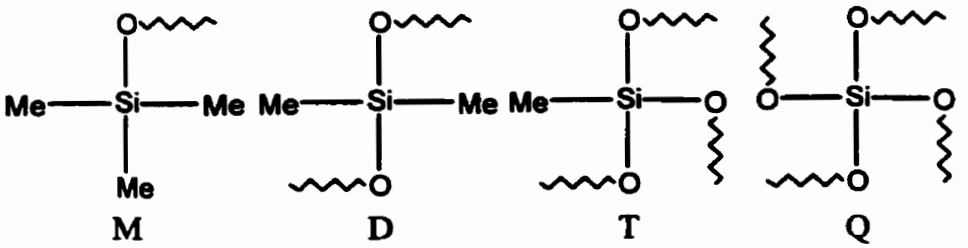


Figure 1.1 Structures of M,D,T and Q siloxane building units where the alkyl groups are methyls.

certain conditions. It has been demonstrated that hydroxy-terminated polydimethylsiloxane (HPDMS) will depolymerize at temperatures > 350 °C [19]. The proposed mechanism of depolymerization proceeds via a cyclic intermediate formed by an intramolecular condensation reaction involving terminal silanols. The depolymerization results predominantly in hexamethylcyclotrisiloxane (D_3) along with lesser amounts of octamethylcyclotetrasiloxane (D_4) and decamethylcyclopentasiloxane (D_5). Polydimethylsiloxane is more thermally stable than HPDMS, requiring temperatures ≥ 430 °C to initiate depolymerization [19]. Again the depolymerization proceeds through the formation of D_3, D_4, and D_5. The presence of an alkaline catalyst will lower the depolymerization temperature by as much as 250 °C [20].

Due to the large number of down-the-drain applications of silicones, questions have arisen as to their environmental impact. Polydimethylsiloxane is nearly insoluble in water and, therefore, tends to be deposited on extracted sewage sludge which is frequently utilized as agricultural fertilizer [21]. Once spread on the soil, PDMS undergoes acid catalysed hydrolytic depolymerization [22-27]. The mechanism of depolymerization is unknown, although there is evidence to suggest that it occurs via both end group and random chain scission [28]. Lehmann *et al.* [23] determined that increasing the moisture content of soil significantly slows the rate of depolymerization. At low moisture levels, PDMS may be coordinated to acid sites on the soil surface. However if the moisture level is high there are fewer sites to which the PDMS can

coordinate and initiate depolymerization.

The dominant major water soluble depolymerization product of PDMS is DMSD [21, 24-26, 29] probably because it is more soluble than all higher molecular weight products and/or condensates. Therefore, DMSD is the main vehicle of silicone contamination in the environment and is also the most likely silicone derivative to be bioactive [30]. Lehmann *et al.* [23] showed that the decomposition of ^{14}C labeled PDMS on soil yields labeled CO_2 along with labeled DMSD. Sabourin *et al.* [30] determined that the CO_2 is formed from degradation of the DMSD by a biological pathway. They concluded that a fungus, *Fusarium oxysporum* Schlechtendahl, and a species of *Arthrobacterer* were capable of mineralizing DMSD to inorganic silicates in both soil samples and liquid cultures when a carbon source was present, although the mechanism by which DMSD is mineralized is unknown [31].

Aqueous Silicate Chemistry

Silicon is almost always four coordinated by oxygen in aqueous systems. The notation system described above for silicones has been adapted to denote the coordination number and the connectivity at silicate Si centres. Here Q, P, and H are used respectively to represent tetra-, penta- and hexaoxo silicon. The number of siloxane linkages on the silicon atom is represented by a superscript. For example, the silicate monomer (SiO_4^{4-}) is represented by Q^0, whereas the dimer ($O_3SiOSiO_3^{6-}$) is denoted as Q^1Q^1or simply as Q^1_2, the subscripted figure indicating the number of

chemically equivalent centres in a symmetrical species.

The solubility of amorphous silica, SiO_2, is relatively low at pH 7, with reported values ranging between 100 and 130 ppm at 25 °C [8]. However, the solubility increases dramatically above pH 9. The main anion present under very dilute and/or highly alkaline conditions is the silicate monomer. The equilibria between the different silicate anions are governed by the rules of polymer chemistry. The number of silicate anions present rises as Si concentration is increased, pH is decreased and/or temperature is decreased. In solutions containing equimolar concentrations of SiO_2 and alkali metal hydroxide there are as many as 30 different silicate anions undergoing rapid chemical exchange with one another [32].

Silicone Medical Implants

Silicone has been used for medical implants since the late 1950's [33]. It was first used for "shunts" to funnel excess fluid away from the brain to the chest cavity. Silicones have since has become an important part of many medical implants including tracheotomy tubes, ocular lenses, artificial heart valves and in devices for reconstructive surgery. Over two million patients had received surgical implants made either partially or entirely of silicone in the United States by 1988 [33].

Although there has never been conclusive evidence linking any disease or illness to silicone medical implants [18,33], widespread fear of silicone, most notably of breast implants, erupted briefly in the 1990's. Many different types of mammary

prostheses incorporate silicone. Single lumen models consist of a single silicone shell filled with silicone gel, saline or soybean oil [18]. Double lumen implants have two silicone shells, the inner shell containing silicone gel and the outer shell holding saline [18]. The concern expressed over the safety of implants is related to silicone gel escaping into the blood system through leakage and/or shell rupture. Indeed, silicone antibodies have been detected in implant recipients [33]. However, silicone antibodies have also been detected in non-implant recipients, demonstrating the ubiquity of silicone in the everyday environment.

In the mid 1990's, Garrido *et al.* [34,35] published a number of reports on the biomigration and degradation of polydimethylsiloxanes. Silicone oil was either injected or implanted into the lower back of rats, and after various delays, tissue and blood samples from the rats were analyzed using ^{1}H NMR and ^{29}Si MAS NMR. They reported resonances corresponding to a great many silicon containing species, and, moreover, that silicone migrated to various organs where it degraded to form silica [34,35]. In addition, they reported silicon concentrations in excess of 100 mM in the blood samples of silicone implant recipients [35].

These reports played a significant role in bringing about a multinational ban of silicone breast implants. Other workers, however, were unable to reproduce Garrido *et al.*'s findings [36]. Measured silicon concentrations were five orders of magnitude less than Garrido's and their reported ^{29}Si NMR resonances could not be detected [25].

In a highly unusual move following intense criticism [37-39], the journal which published most of the Garrido work reassessed their data and declared " none of the Garrido group's papers should have been published" [40].

Silicon-29 NMR

Silicon-29 NMR is a very useful tool for determining the chemistry of silicon in different environments. However, the natural isotopic abundance of ^{29}Si is only 4.7%. To obtain spectra with reasonable signal to noise, it is therefore necessary to employ a) numerous pulse acquisitions, b) highly concentrated solutions, and/or c) ^{29}Si enrichment. The low natural isotopic abundance of ^{29}Si also precludes the detection of ^{29}Si-^{29}Si coupling, a potential source of structural information. Moreover, the silicon nucleus tends to undergo slow longitudinal (T_1) relaxation, necessitating extremely long periods of acquisition.

Another potential source of structural information is ^{1}H-^{29}Si scalar coupling. Unfortunately, rapid chemical exchange with water protons prevents the detection of *J*-coupling involving attached hydroxyl groups. Nevertheless, two or three bond ^{1}H-^{29}Si coupling from attached aliphatic or alkoxy groups can often be detected. If the magnitude of ^{1}H-^{29}Si coupling is sufficiently large, DEPT-NMR experiments can be performed which greatly enhance the signal to noise ratio and significantly lessen the overall acquisition period [41]. When acquiring conventional ^{29}Si ^{1}H-decoupled spectra the ^{1}H signal must be carefully gated in order to avoid signal loss caused by the

nuclear Overhauser effect. (Here, nOe is detrimental since ^{1}H and ^{29}Si have gyromagnetic ratios of opposite sign.)

The overall spectral window for ^{29}Si chemical shifts is about 400 ppm, although most species are clustered over a range of about 200 ppm. Regions corresponding to M, D, T, Q, P, and H units are spread out over this 200 ppm frequency range and, for solution species, do not generally overlap.

Chapter 2-Experimental

Reagents

Type I deionized/distilled water (DDW) which had been passed through an organic removal cartridge (Barnstead E-Pure) and filtered (0.2 μm) was used throughout the study. The silicon concentration of the DDW and of the deuterated water (D_2O) used to provide a NMR frequency lock was less than the ICP (Jarell Ash 9000) detection limit of 2 mg L^{-1}.

All plastic labware was cleaned by successively soaking in 10% nitric acid, 10% hydrochloric acid, 0.01 M Na_2H_2EDTA and, finally, DDW. Samples were prepared and stored in 15 mL or 30 mL low density polyethylene (LDPE) bottles prior to analysis. All aqueous solutions were transferred using non-lubricated LDPE syringes in conjunction with Teflon needles. Sample containers which had come into contact with silicone material in the study were subjected to three successive rinsings with toluene prior to the aforementioned cleansing procedure.

Most of the organosilicon compounds were obtained commercially. See Table 2.1. A silicone gel filled mammary prosthesis (Dow Corning, SILASTIC® II brand, catalogue number P01-0300, 300 cc) was generously donated by DOW Corning Ltd., along with a corresponding empty prosthesis shell (0.43 mm thick film), here cut into 3 x 3 mm squares. Dimethylsilanediol was prepared using a method similar to that of Varaprath *et al.* [21]. Approximately 16 g of DDW was mixed with 25 g of dimethoxydimethylsilane (DMDMS) in a 250 mL round bottomed flask and stirred

using a magnetic stir bar until the two phase mixture was homogeneous. Methanol and most of the water were removed on a rotary evaporator at approximately 60 °C until a white solid was obtained. The resulting solid was immediately washed with hexanes and filtered to obtain a white fluffy solid which was recrystallized using hot acetone. The resulting DMSD crystals were used immediately for sample preparation, that is, before they underwent polymerization. Amorphous silicon dioxide was prepared by the hydrolysis of high purity silicon tetrachloride (Table 2.1). The resulting silica gel was dried, crushed and washed to a neutral pH.

Human blood plasma was collected from two anonymous donors having no silicone implants. The blood was collected in glass, additive-free, blood collection tubes (Becton Dickinson model number L43209PT) and centrifuged within 10 minutes to separate out the blood cells. The plasma was then transferred to a clean LDPE bottle. Alternatively, serum was collected by allowing the blood to clot prior to centrifuging.

Sample Preparation for Silicone Degradation Study

Between 0.7 to 2.0 g of HMDS, PDMS, HPDMS, MPDMS, triethylsilanol (TES), prosthesis gel or shell were added to LDPE bottles containing 20 g of (a) water (b) 6.5 mol kg^{-1} sorbitol, (c) 0.01 mol kg^{-1} NaOH (d) 5.6 mol kg^{-1} NaOH, 6.2 mol kg^{-1} sorbitol or (e) 0.01 mol kg^{-1} HCl. Alternatively, 1.0 ± 0.5 g of silicon compound was added to 2 to 6 g of (f) plasma or (g) serum. In some cases large scale samples

(approximately 7 g of silicone and 120 g of solvent) were prepared. The aqueous phase of all samples contained a minimum of 15 wt% D_2O to provide a NMR field frequency lock. See Table 2.2. The samples were tumbled end over end on a rotating stage at 37 °C for period ranging from 2.5 to 34 months. The aqueous fractions were filtered using 0.1 μm centrifuge filters (Millipore Ultrafree-CL, low binding Durapore membrane) at 3000 rpm to remove colloidal material and then transferred to a clean LDPE bottle. The samples were then analyzed using NMR spectroscopy.

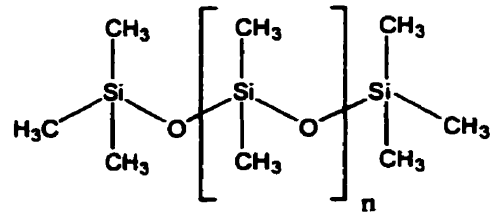
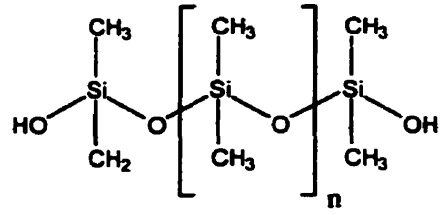
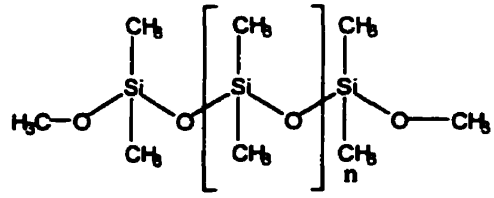
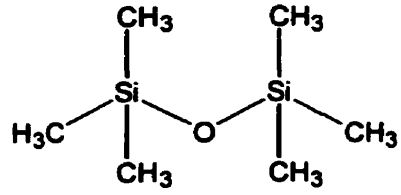
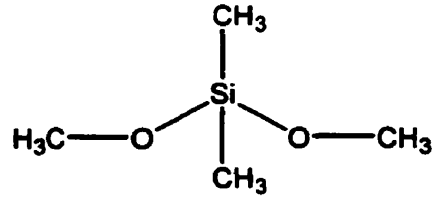
NMR Measurements

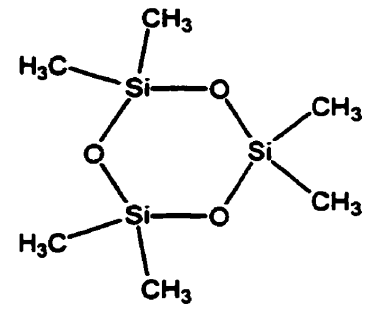
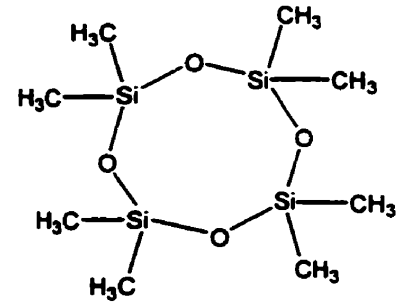
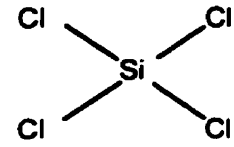
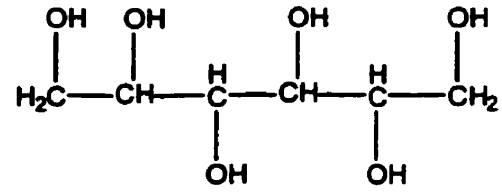
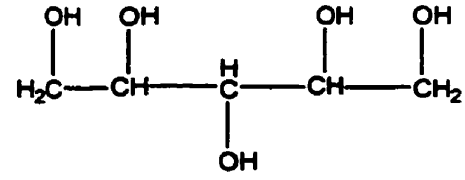
Silicon-29 NMR spectra of the aqueous fractions were acquired on Bruker AMX 500 (University of Manitoba), Varian Inova 500 (Lakehead University) and Varian Inova 750 (Keck NMR facility, University of Illinois at Urbana-Champaign) NMR spectrometers operating at 99.31, 99.28 and 149.00 MHz, respectively. Glass coil supports in the AMX 500 probehead were replaced with Vespel SP-1 polyimide components in order to eliminate ^{29}Si background signals. To avoid chemical contamination the samples were contained in Teflon FEP NMR tube liners (sealed with Teflon TFE caps) or thin-wall Kel-F NMR tubes. Silicon-29 DEPT-45 experiments were performed to enhance the signal from Si nuclei coupled to protons (consequently, ^{29}Si DEPT-45 NMR spectra were non-quantitative). Some spectra were also obtained at 6 °C to optimize signal sensitivity. All spectra were referenced to an external TMS standard.

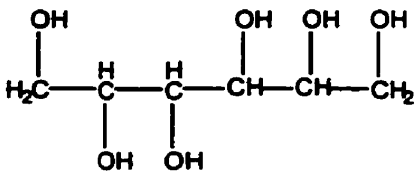
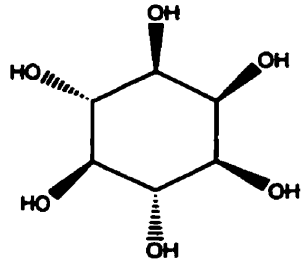
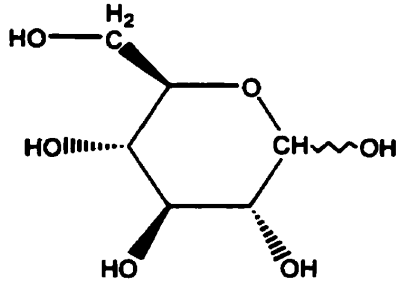
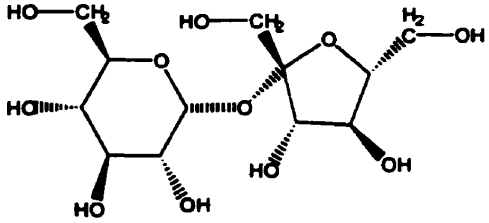
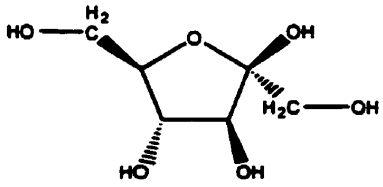
Proton NMR spectra were performed on the Varian Inova 500 NMR spectrometer operating at 499.72 MHz. The water signal was suppressed using a presaturation pulse sequence to facilitate the detection of minor ^{1}H resonances.

The concentration of hydrolysis products was determined using ^{1}H NMR spectroscopy. The integrated area of the resonance at *ca.* 0 ppm corresponding to dimethylsiloxane (D) centres was compared to that of the methyl resonance at 0.9 ppm of propanol which was added as an internal integration standard. A presaturation pulse sequence was used to suppress the ^{1}H water signal. The dimethylsiloxane and propanol methyl resonances were sufficiently far removed such that they were unaffected by suppression of the water signal.

Table 2.1 List of chemical reagents employed in this study.

Reagent	Supplier/purity	Structure
PDMS	Aldrich 100 cSt	
HPDMS	Aldrich 90-150 cSt	
MPDMS	Aldrich $M_w \approx 27000$	
HMDS	Aldrich/99.5%	
TES	Aldrich/97%	$Si(C_2H_5)_4$
DMDMS	Aldrich/95%	

Reagent	Supplier/purity	Structure
D_3	Aldrich/98%	
D_4	Aldrich/98%	
silicon tetrachloride	Aldrich/99.998%	
sorbitol	Aldrich/97%	
xylitol	Aldrich/98%	

Reagent	Supplier/purity	Structure
mannitol	Aldrich	
myo-inositol	Aldrich/95%	
glucose	Aldrich/99%	
sucrose	Caledon	
fructose	Aldrich/99%	

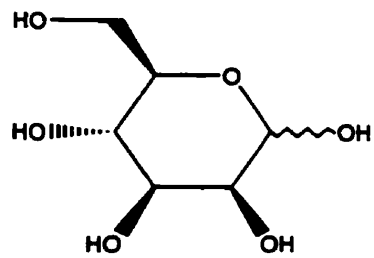
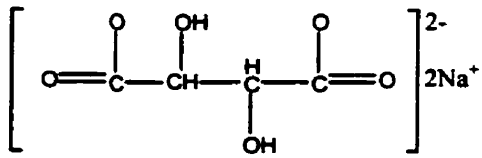
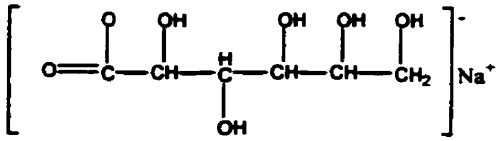
Reagent	Supplier/purity	Structure
mannose	Aldrich/99%	
NaOH	Aldrich/99.99%	
Na-Tartrate	Aldrich/99+% dihydrate	
Na-Gluconate	Aldrich/97%	
D_2O	Cambridge/ 99.9%, Aldrich/99.9%	

Table 2.2 Amount of silicone added to the different decomposition medium.

Silicone	Decomposition medium	Weight added /g	Weight of solvent[a] /g
HPDMS	NaOH	7.03	121
PDMS		7.12	115
MPDMS	NaOH-Sorbitol	1.44	9.27
HPDMS	Plasma	1.23	5.35
Silicone Shell		0.727	6.95
Silicone Gel		1.94	6.67
HMDS		1.10	4.23
MPDMS		0.860	4.95
PDMS		1.54	5.05
Blank		0	4.66
HPDMS	Serum	1.13	3.70
MPDMS		1.02	4.22

[a] The mass shown only includes the mass of the solvent used in the solution, not the added solute components. The plasma and the serum were assumed to consist entirely of water.

Chapter 3-Results

3.1 ^{29}Si Analysis of Silicone Degradation

A. Assignment of ^{29}Si Resonances

In principle, silicon-29 NMR is an ideal tool for the speciation of silicone depolymerization products. The concentration of hydrolysis products was frequently well below the detection limits of conventional $\{^1H\}$-^{29}Si NMR spectroscopy and, therefore, DEPT-45 ^{29}Si NMR was employed. However, since the most probable products all contain the same building unit, $Si(CH_3)_n$, DEPT provides little structural information. Speciation must therefore be based on chemical shift comparisons with model compounds and on the observed dependence of chemical shifts on solution conditions such as solvent composition, T and pH. Silicon-29 chemical shift data for low molecular weight silanols have primarily been reported for the pure compounds and for non-aqueous solutions [21,42]. Consequently, the ^{29}Si chemical shift *in water* of potential hydrolysis products had to be determined. A comparison of literature and experimental data is presented in Table 3.1.

The addition of synthesized DMSD to 50 wt% aqueous acetone yields a ^{29}Si resonance at -0.78 ppm with respect to an internal TMS standard. Under strictly *aqueous* conditions, a 0.014 mol kg^{-1} DMSD solution yields one signal at -0.17 ppm relative to external TMS. A second signal also appears in spectra of freshly prepared solutions with > 0.04 mol kg^{-1} DMSD, apparently corresponding to the dimer,

tetramethyldisiloxanediol (TMDSD). Indeed, the *ca.* 8 ppm difference in shift between DMSD and TMDSD peaks is essentially equal to that separating the resonances of monomeric and dimeric silicate ions. However, there is a *ca.* 4 ppm difference between literature and experimental chemical shifts of DMSD and TMDSD. The discrepancies are caused by the different solvent compositions, *i.e.*, pH and temperature differences [43].

Dilute aqueous solutions of D_3 and D_4 yielded ^{29}Si NMR signals at -9.02 and -19.86 ppm, respectively. These shifts are very close to those obtained for D_3 and D_4 in acetone, as one might expect given the absence of H-bonding silanol groups on these ring species.

The chemical shift of DMSD is highly dependent upon the pH of solution and the temperature at which NMR spectra are acquired, varying by as much as 1 ppm.

The DEPT-45 ^{29}Si NMR spectra of the polymers in deuterated toluene demonstrated that signals corresponding to D-units in the polymer chain at *ca.* -23.70 ppm are present. In addition, resonances from the terminal substituents on MPDMS and PDMS are observed at -13.85 and 5.38 ppm respectively. There is no evidence for any other silicon species.

Table 3.1 Literature and experimental ^{29}Si NMR chemical shifts (ppm) of organosilicon compounds with respect to TMS.

Species	Literature values	Experimental values in water (or 50 % wt acetone)
HMDS	6.79[a]	
DMSD	3.9[b] (–6[c])	–0.17 (–0.78)
TMDSD	–4.2[b] (–13 to –14[c])	–8.07
D units	–15 to –23[a]	
D_3	–9.12[a]	–9.02
D_4	–19.51[a]	–19.86
D_5	–22[a]	
D_6	–23[a]	
T units	–62 to –68[a]	
$[(RO)Me_2Si]_2O$	–7 to –12[c]	
$[(RO)_2MeSi]_2O$	–42 to –55[c]	
$MeSi(OEt)_3$	–42.1[d]	
$MeSi(OEt)_2(OH)$	–40.4[d]	
$MeSi(OEt)(OH)_2$	–39.0[d]	
$MeSi(OH)_3$	–37.8[d]	
$MeSi(OMe)_3$	–38.2	
$MeSi(OMe)_2(OH)$	–38.1	
$MeSi(OMe)(OH)_2$	–38.1	
$MeSi(OH)_3$	–38.4	
$Me_2Si(OEt)_2$	–3.8[d]	
$Me_2Si(OEt)(OH)$	–3.4[d]	
$Me_2Si(OH)_2$	–4.2[d]	

Species	Literature values	Experimental values in water (or 50 % wt acetone)
$Me_2Si(OMe)_2$	1.2	
$Me_2Si(OMe)(OH)$	–1.5	
$Me_2Si(OH)_2$	–4.1	

[a] from ref. 44, solvent = acetone. [b] from ref. 42, solvent = H_2O. [c] from ref. 21, solvent = acetone [d] from ref. 43, solvent = 3 parts water one part ethanol. [e] from ref. 43, solvent = 3 parts water one part methanol.

B. Silicones in Pure Water

None of the silicones in Table 2.1 yielded a single detectable ^{29}Si NMR signal following tumbling in water at 37 °C for periods of up to *2.5 months*.

C. Silicones in 6.5 mol kg^{-1} Sorbitol

Similarly, none of the silicones in Table 2.1 yielded a single detectable ^{29}Si NMR signal upon tumbling in aqueous sorbitol at 37 °C for periods of up to *2.5 months*.

D. Silicones in 0.01 mol kg^{-1} NaOH

(i) Hexamethyldisiloxane (HMDS)

After 0.01 mol kg^{-1} NaOH was tumbled with HMDS for *2.5 months* at 37 °C the expected hydrolysis product, trimethylsilanol, was not detected. However, a signal at –0.89 ppm that is consistent with DMSD was resolved using ^{29}Si DEPT-45 NMR.

See Figure 3.1a. Dimethylsilanediol could only result from cleavage of trimethylsilyl groups. By contrast, after *4 months* of tumbling at 37 °C a signal was observed at 18.65 ppm, consistent with trimethylsilanol. However, previous work by Schach and Kinrade [45] showed that sodium trimethylsilanoate added to pure water resulted in immediate condensation to HMDS. In neither case did ^{29}Si-{^{1}H} NMR reveal the presence of dissolved silicates.

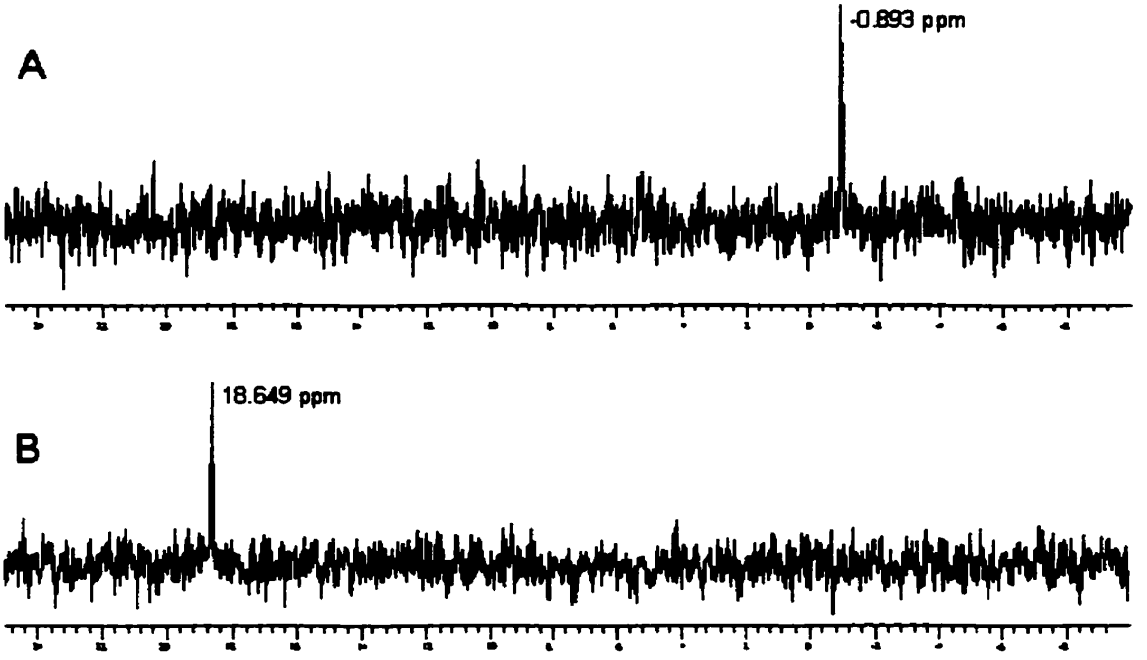


Figure 3.1 (A) DEPT–45 ^{29}Si NMR spectrum (99.32 MHz) at 6 °C of 0.01 mol kg^{-1} NaOH tumbled with HMDS for 2.5 months at 37 °C. 11000 repetitions. Recycle time = 15 s. Artificial linebroadening = 1.0 Hz. (B) DEPT–45 ^{29}Si NMR spectrum (99.32 MHz) at 6 °C of 0.01 mol kg^{-1} NaOH tumbled with HMDS for 4 months. 9052 repetitions. Recycle time = 15 s. Artificial linebroadening = 1.0 Hz.

(ii) Polydimethylsiloxane (PDMS)

The ^{29}Si DEPT NMR spectrum in Figure 3.2 reveals that PDMS hydrolysed after tumbling *2.5 months* in 0.01 mol kg^{-1} NaOH at 37 °C. The major signal at –1.30 ppm is consistent with DMSD, whereas the smaller signal at –23.05 ppm apparently corresponds to a D-centre in some oligomeric decomposition product. Remarkably, there is no trace of Si- containing species after *26 months* of tumbling. In neither case did conventional ^{29}Si-{^{1}H} NMR reveal the presence of dissolved silicates.

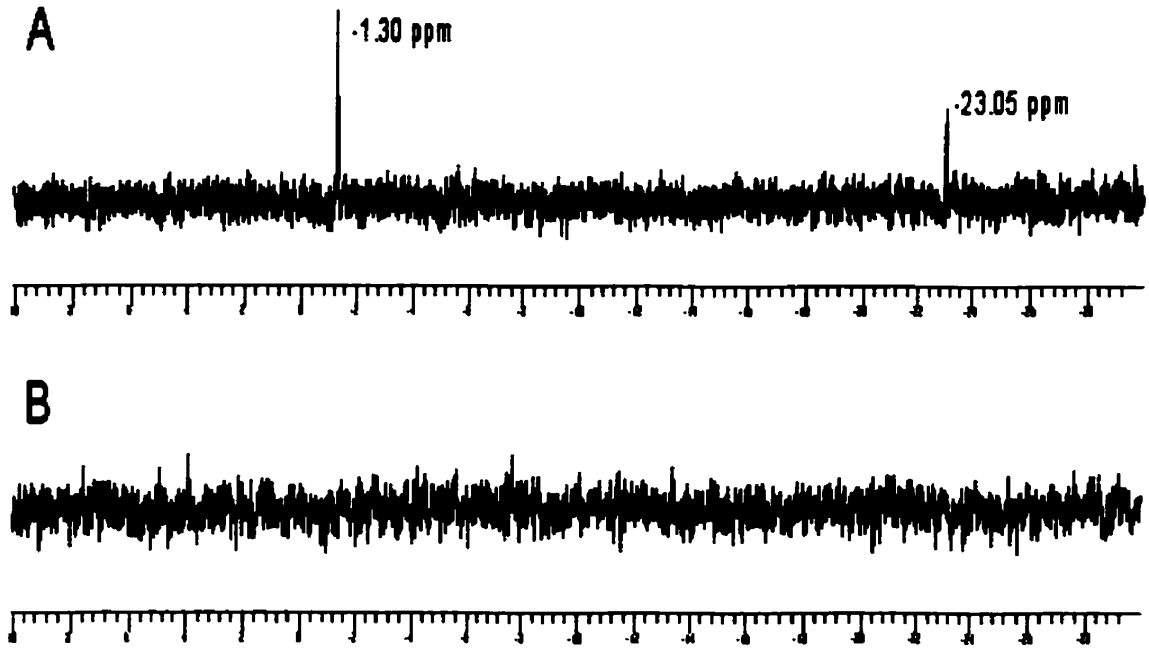


Figure 3.2 (A) DEPT–45 ^{29}Si NMR spectrum (149.00 MHz) at 6 °C of 0.01 mol kg^{-1} NaOH tumbled with PDMS for 2.5 months at 37 °C. 956 repetitions. Recycle time = 6 s. Artificial linebroadening = 1.0 Hz. (B) DEPT–45 ^{29}Si NMR spectrum (99.28 MHz) at 6 °C of 0.01 mol kg^{-1} NaOH tumbled with PDMS for 24 months at 37 °C. 2300 repetitions. Recycle time = 10 s. Artificial linebroadening = 1.0 Hz.

(iii) Hydroxy-terminated polydimethylsiloxane (HPDMS)

HPDMS also hydrolysed when tumbled in 0.01 mol kg^{-1} NaOH for *2.5 months* at 37 °C. However, the only detectable ^{29}Si resonance was that of DMSD at –0.87 ppm. A considerably higher concentration of DMSD plus a trace amount of TMDSD is evident after *24 months* of tumbling. Once again, ^{29}Si-{^{1}H}NMR spectroscopy failed to detect the presence of dissolved silicates.

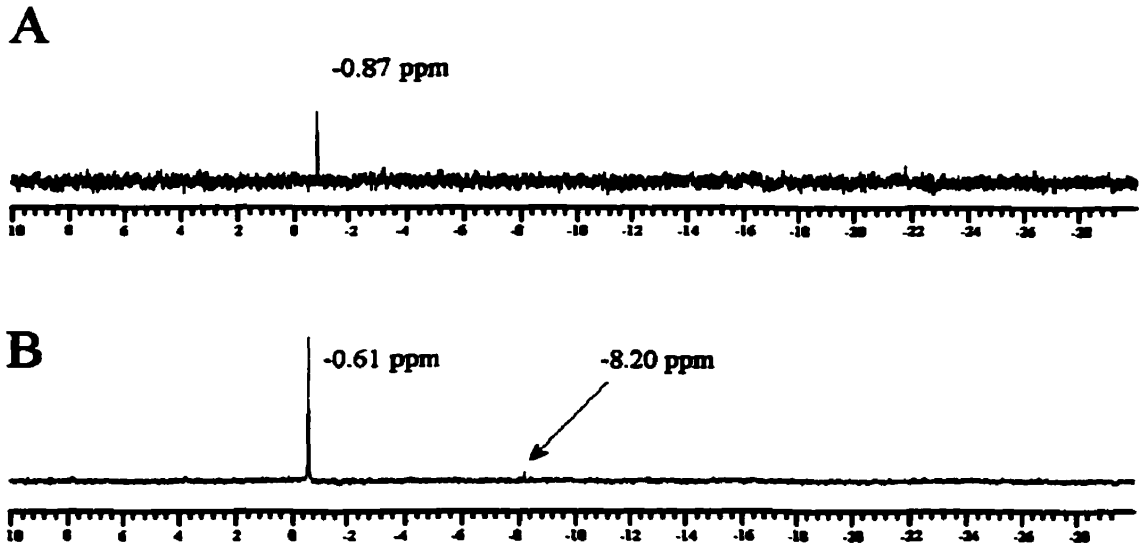


Figure 3.3 (A) DEPT-45 ^{29}Si NMR spectrum (99.31 MHz) at 27 °C of 0.01 mol kg^{-1} NaOH tumbled with HPDMS for 2.5 months at 37 °C. 3520 repetitions. Recycle time = 20 s. Artificial linebroadening = 1.0 Hz. (B) DEPT-45 ^{29}Si NMR spectrum (99.28 MHz) at 6 °C of 0.01 mol kg^{-1} NaOH tumbled with HPDMS for 24 months at 37 °C. 3000 repetitions. Recycle time = 6 s. Artificial linebroadening = 1.0 Hz.

(iv) Methoxy-terminated polydimethylsiloxane (MPDMS)

Methoxy-terminated polydimethylsiloxane tumbled in 0.01 mol kg^{-1} NaOH for *2.5 months* at 37 °C also results in only a very strong signal consistent with DMSD in the aqueous fraction. See Figure 3.4. As with the other silicones investigated, ^{29}Si-{^{1}H}NMR spectroscopy failed to detect the presence of dissolved silicates. Long term tumbling periods were not investigated.

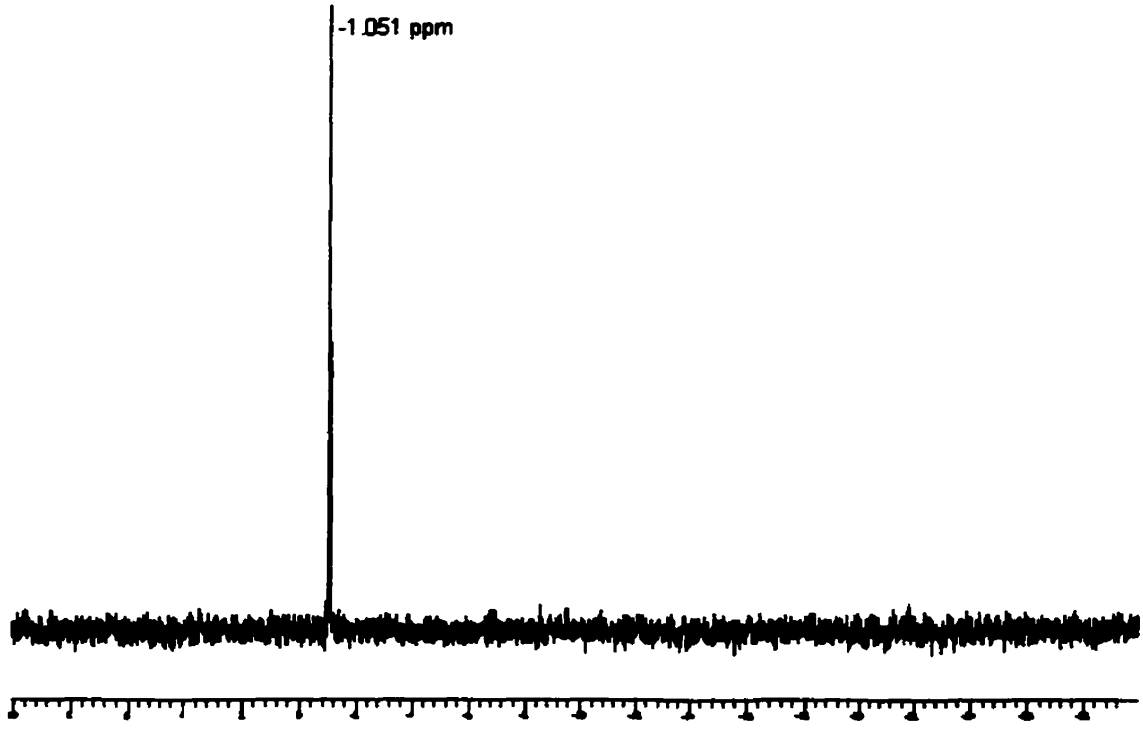


Figure 3.4 DEPT–45 ^{29}Si NMR spectrum (149.00 MHz) at 10 °C of 0.01 mol kg^{-1} NaOH tumbled with MPDMS for 2.5 months at 37 °C. 1856 repetitions. Recycle time = 10 s. Artificial linebroadening = 1.0 Hz.

(v) Mammary prosthesis

Figure 3.5 shows that silicone from both the gel interior and elastomeric shell of the Dow Corning SILASTIC II prosthesis hydrolysed to DMSD after tumbling in 0.01 mol kg^{-1} NaOH for *26 months* at 37 °C. No other species, including inorganic silicates, could be detected.

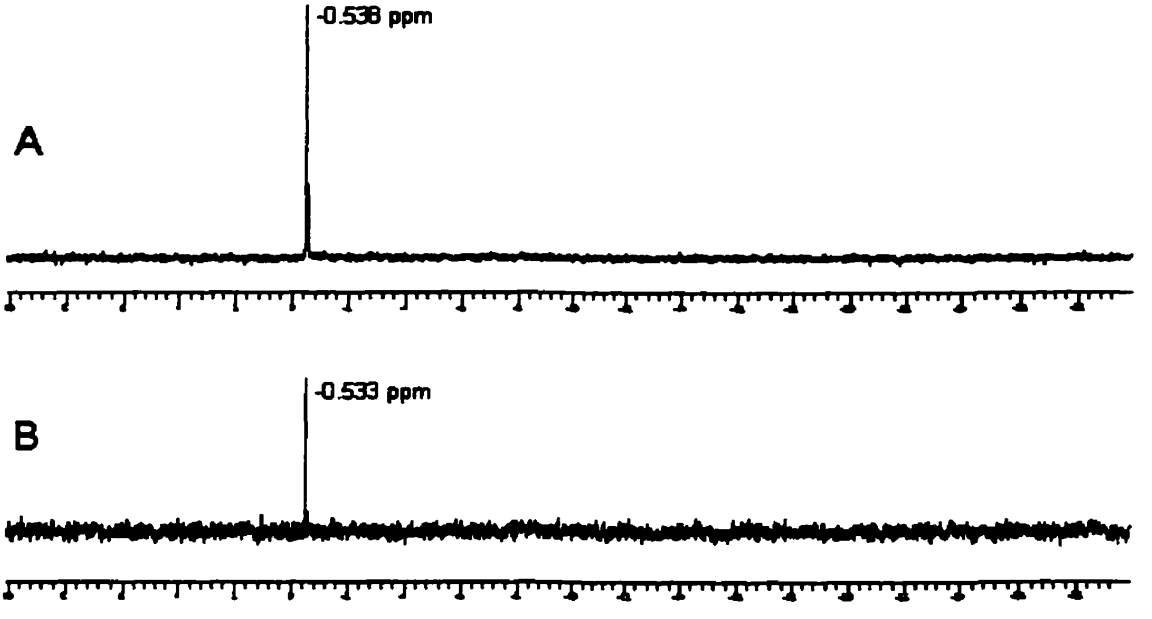


Figure 3.5 (A) DEPT-45 ^{29}Si NMR (99.31 MHz) spectra at 27 °C of (A) 0.01 mol kg^{-1} NaOH tumbled with implant contents for 26 months. (B) 0.01 mol kg^{-1} NaOH tumbled with implant shell for 26 months. Each spectrum was acquired with 10000 pulse repetitions and a recycle time of 15 s. Artificial linebroadening = 1Hz.

E. Silicones in 0.01 mol kg^{-1} HCl

Polydimethylsiloxane tumbled for *26 months* at 37 °C in 0.01 mol kg^{-1} HCl solution yielded a relatively ^{29}Si resonance at –0.26 ppm consistent with DMSD. No other signals were observed. See Figure 3.6.

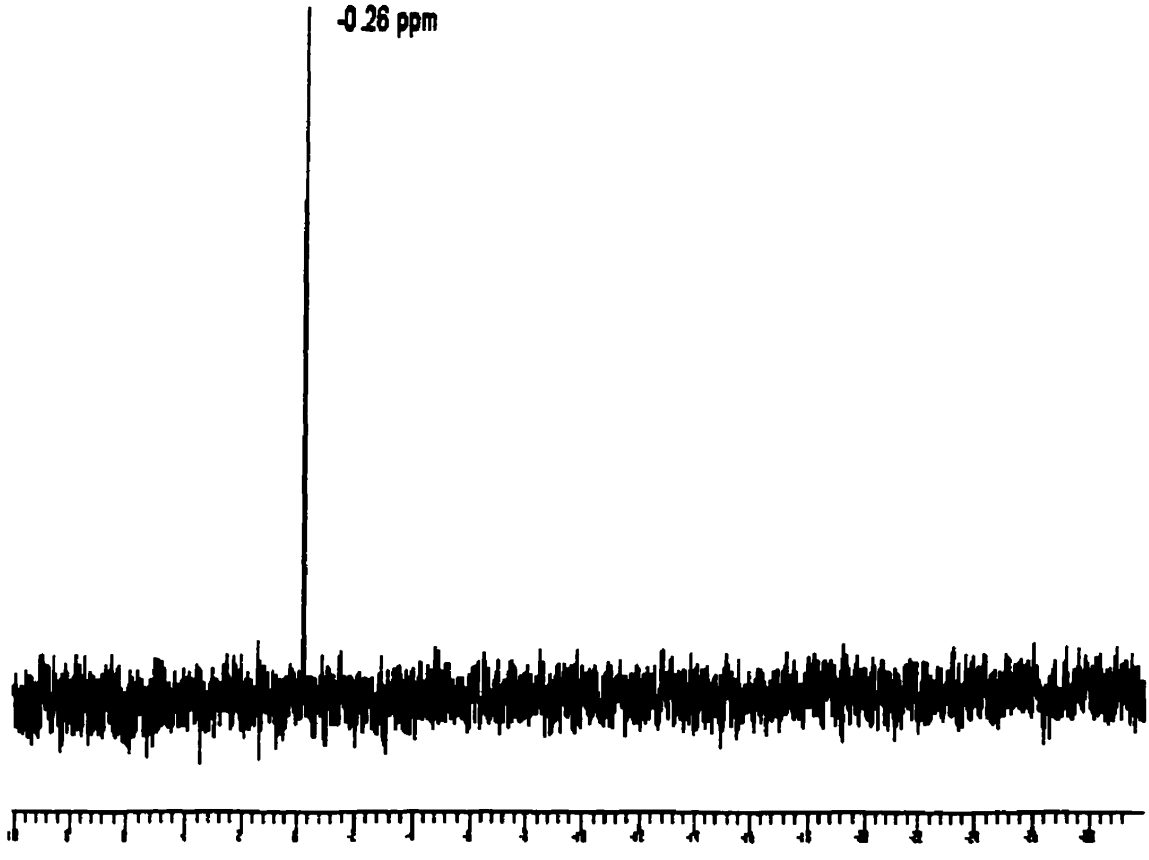


Figure 3.6 DEPT–45 ^{29}Si NMR spectra (99.35 MHz) at 27 °C of 0.01 mol kg^{-1} HCl tumbled with PDMS for 26 months. 10000 repetitions. Recycle time = 15 s. Artificial linebroadening = 1.0 Hz.

F. Silicones in blood

(i) Hexamethyldisiloxane (HMDS)

When HMDS was tumbled in human blood plasma for *11 weeks* at 37 °C a remarkable observation was made. Two products that would result from methyl cleavage of HMDS are observed. Silicon-29 NMR peaks at 0.06 and –71.85 ppm consistent with DMSD and silicic acid, respectively, were detected. See Figure 3.7. This demonstrates the possibility of methyl cleavage of silicones in biological matrices and that the ultimate degradative fate of silicones may be inorganic silicates.

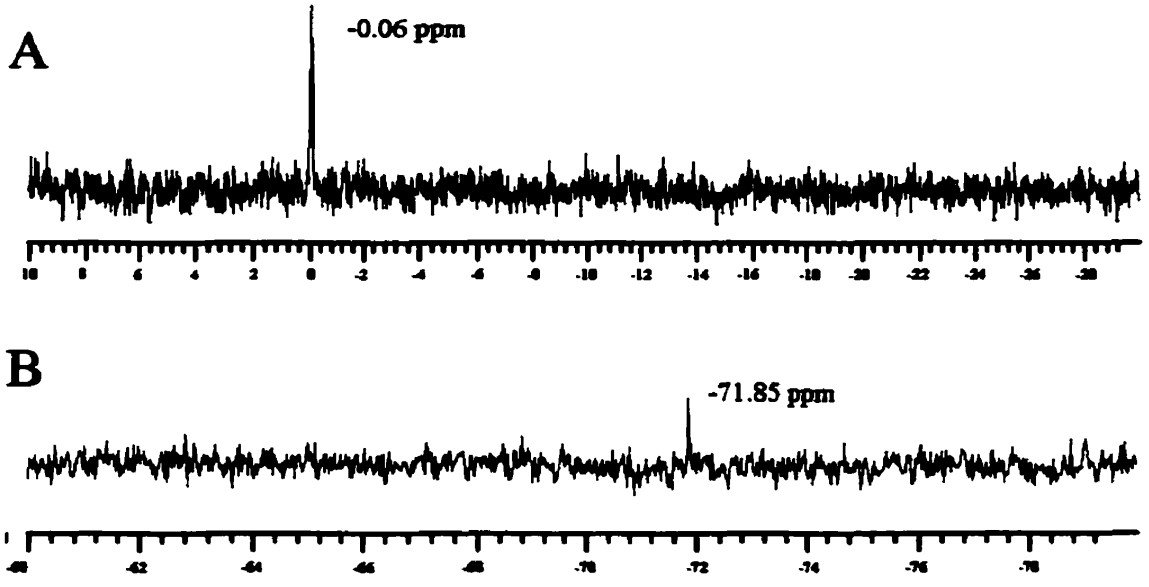


Figure 3.7 (A) DEPT-45 ^{29}Si NMR spectrum (99.31 MHz) at 27 °C of HMDS tumbled in plasma for 11 weeks at 37 °C. 5000 repetitions. Recycle time = 15 s. Artificial linebroadening = 1.0 Hz. (B) Inverse gated proton decoupled ^{29}Si NMR spectrum of HMDS tumbled in plasma for 11 weeks at 37 °C. 466 repetitions. Recycle time = 180 s. Artificial linebroadening = 1 Hz.

(ii) Polydimethylsiloxane (PDMS)

When PDMS was tumbled in human blood plasma at 37 °C for *4 months* and analysed by ^{29}Si NMR, there was no evidence for the presence of silicone hydrolysis products. However, after *26 months* of tumbling the only identifiable signal was that at –23.0 ppm corresponding to D-units in a silicone oligomer (as was detected for PDMS in 0.01 mol kg^{-1} NaOH). See Figure 3.8. ^{29}Si-{^{1}H}NMR spectroscopy failed to detect the presence of dissolved silicates.

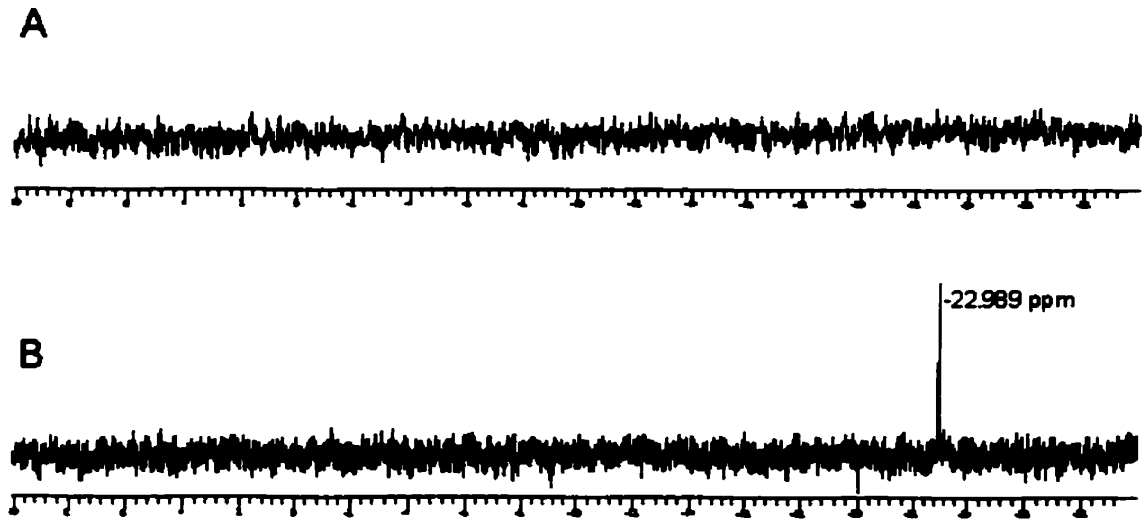


Figure 3.8 (A) DEPT–45 ^{29}Si NMR spectrum (99.31 MHz) at 6 °C of PDMS tumbled in plasma for 4 months at 37 °C. 3035 repetitions. Recycle time = 15 s. Artificial linebroadening = 1.0 Hz. (B) DEPT–45 ^{29}Si NMR spectrum (149.00 MHz) at 20 °C of PDMS tumbled in plasma for 26 months. 720 repetitions. Recycle time = 10 s. Artificial linebroadening = 1.0 Hz.

(iii) Hydroxy-terminated polydimethylsiloxane (HPDMS)

Figure 3.9 shows that HPDMS hydrolysed to DMSD when tumbled in human blood plasma at 37 °C for *4 months*. As in the case of PDMS, after *26 months* of tumbling, a resonance consistent with an oligomeric D-centre was also observed. However, DMSD still accounted for *ca.* 60 % of the dissolved silicon. ^{29}Si-{^{1}H}NMR spectroscopy failed to detect the presence of dissolved silicates.

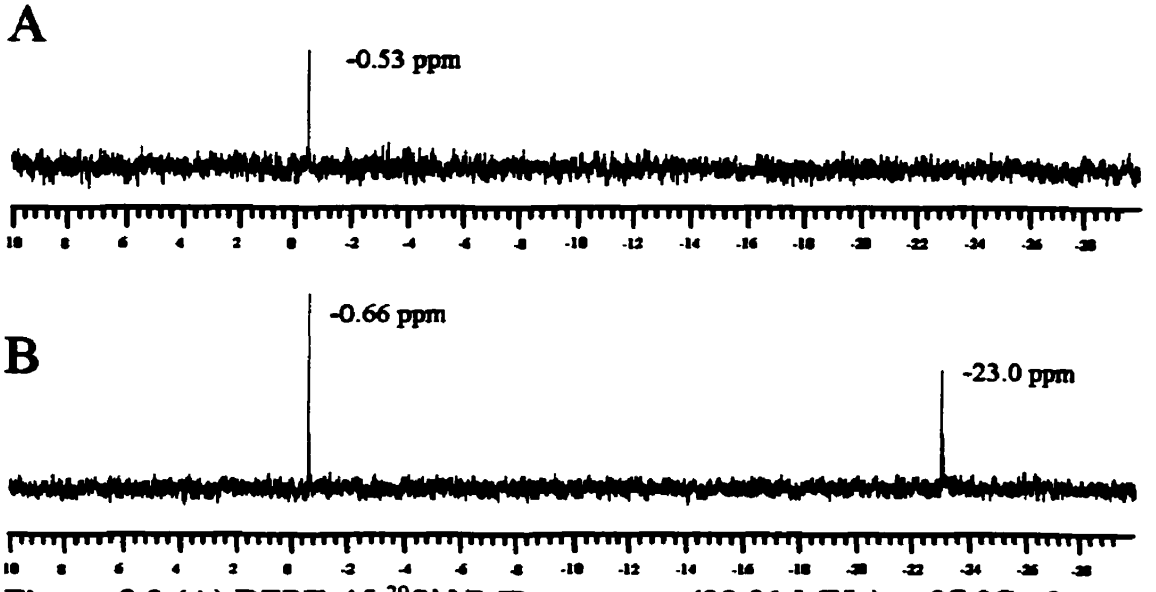


Figure 3.9 (A) DEPT-45 ^{29}Si NMR spectrum (99.31 MHz) at 27 °C of blood plasma tumbled with HPDMS for 4 months. 4148 repetitions. Recycle time = 15 s. Artificial linebroadening = 1 Hz. (B) DEPT-45 ^{29}Si NMR spectrum (99.31 MHz) at 20 °C of blood plasma tumbled with HPDMS for 26 months. 3656 repetitions. Recycle time = 10 s. Artificial linebroadening = 1 Hz.

(iv) Methoxy-terminated polydimethylsiloxane (MPDMS)

Methoxy-terminated polydimethylsiloxane also hydrolysed to DMSD after tumbling in human blood plasma at 37 °C for 4 months. However, Figure 3.10 reveals that after *26 months* the major decomposition product was the oligomeric D-centre, while only a trace of DMSD was evident.

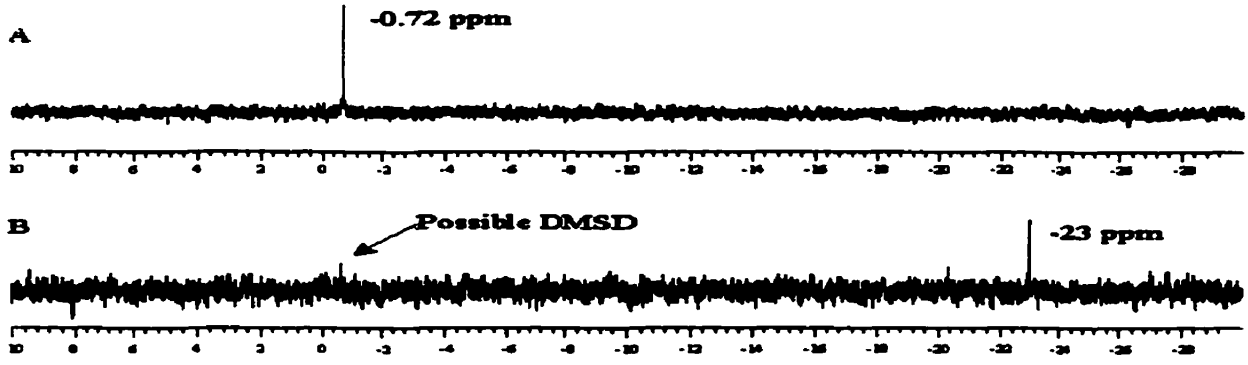


Figure 3.10 (A) DEPT–45 ^{29}Si NMR spectrum at 20 °C of blood plasma tumbled with MPDMS for 4 months. 3008 repetitions. Recycle time = 10 s. Artificial linbroadening = 1 Hz.(B) DEPT–45 ^{29}Si NMR spectrum at 20 °C of blood plasma tumbled with MPDMS for 26 months. 4392 repetitions. Recycle time = 10 s. Artificial linbroadening = 1 Hz.

(v) Mammary prosthesis

After *30 months* of tumbling, the implant interior produced no detectable hydrolysis products. The shell, however, yielded a resonance at –22.77 ppm consistent with the D-containing species. See Figure 3.11. Similar to the other polymers, the implant material yielded no evidence of dissolved silicates.

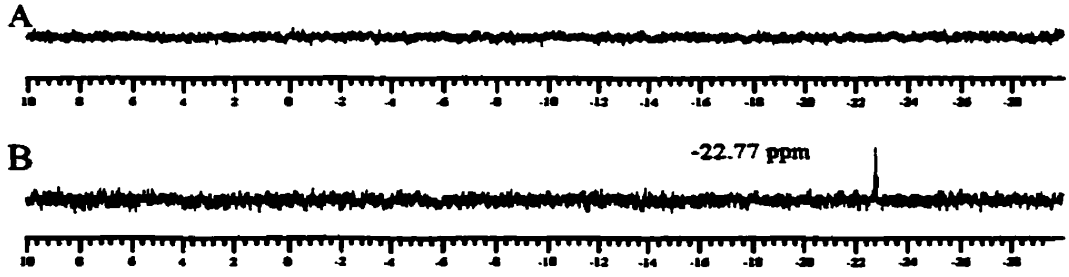


Figure 3.11 (A) DEPT-45 ^{29}Si NMR spectrum (99.28 MHz) at 22 °C of blood plasma tumbled with implant contents for 30 months. 992 repetitions. Recycle time = 10 s. Artificial linebroadening = 1 Hz. (B) DEPT-45 ^{29}Si NMR spectrum (99.28 MHz) at 20 °C of blood plasma tumbled with implant shell for 30 months. 3500 repetitions. Recycle time = 10 s. Artificial linebroadening = 1 Hz.

(vi) Further observations on the interaction of plasma with silicon containing molecules

It is well known that silica surfaces trigger blood coagulation [8]. This phenomenon is commonly utilized in commercial serum collection tubes. In the present study, it was observed that the formation of a fibrin plug (*i.e.*, a blood clot without blood cells) correlated closely with the known presence of aqueous species containing silanol groups. The plug formed almost immediately with added silicate

or TES. Samples that eventually yielded ^{29}Si NMR resonances corresponding to DMSD (or D-containing oligomer) yielded a fibrin plug over time. Thus, the appearance of a fibrin plug was taken to be a good indication that polymer hydrolysis had occurred.

G. Silicones in 5.6 mol kg^{-1} NaOH and 6.5 mol kg^{-1} sorbitol

(i) Polydimethylsiloxane (PDMS)

When PDMS was tumbled for 1 month in an alkaline sorbitol solution (5.6 mol kg^{-1} NaOH, 6.2 mol kg^{-1} sorbitol) DMSD and TMDSD were not detected in the aqueous fraction. However, two new ^{29}Si resonances at –13.22 and –43.82 ppm were detected. See Figure 3.12a. It seems likely that the signals correspond to dimethylsilanol-sorbitol complexes containing either tetraoxo- (–13.22 ppm) or pentaoxosilicon (–43.82 ppm) centres. However, there is little evidence by which assignment of these resonances may be made.

(ii) Hydroxy-terminated polydimethylsiloxane (HPDMS)

When HPDMS was tumbled in the alkaline sorbitol solution, similar results were obtained. See figure 3.12b. Silicon-29 NMR resonances at –13.42, –20.74 and –44.01 ppm were observed. Again the resonances at *ca.* –13 and –44 ppm are consistent with tetraoxo- and pentaoxosilicon dimethylsilanol-sorbitol complexes, and that at –20.74 correlates with a D-centre.

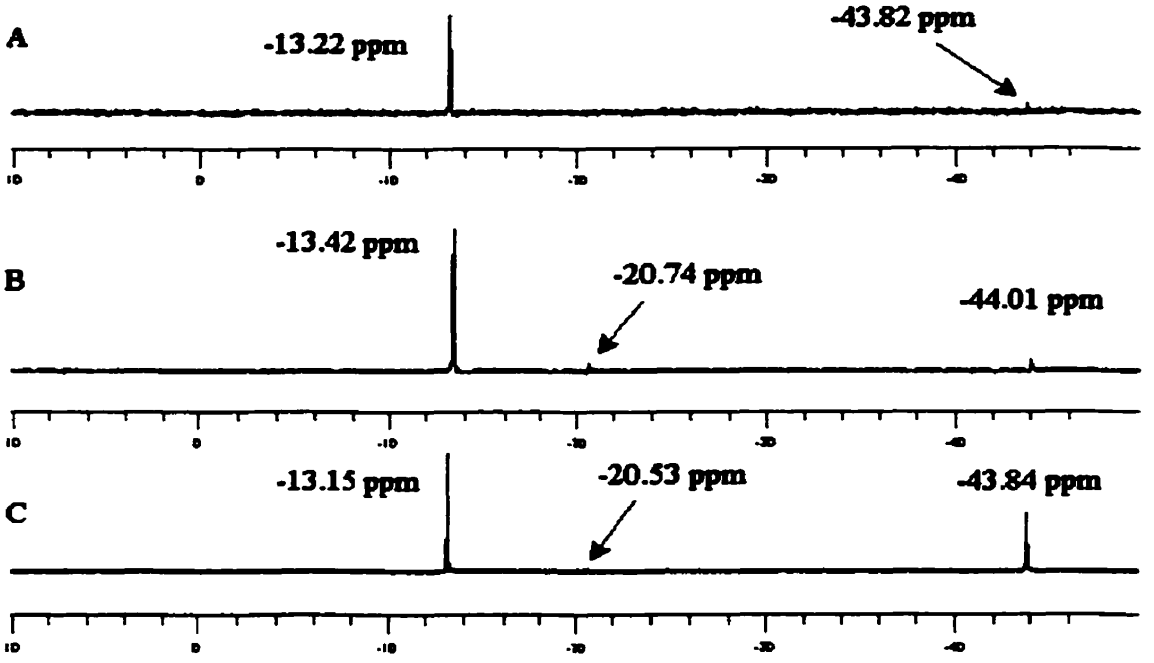


Figure 3.12 (A) DEPT-45 ^{29}Si NMR spectrum (149.00 MHZ) at 6 °C of NaOH/sorbitol tumbled with PDMS for 1 month. 5632 repetitions. Recycle time = 6 s. Artificial linebroadening = 1 Hz. (B) DEPT45 ^{29}Si NMR spectrum (149.00 MHz) at 6 °C NaOH/sorbitol tumbled with HPDMS for 1 month. 2404 repetitions. Recycle time = 6 s. Artificial linebroadening = 1 Hz. (C) DEPT-45 ^{29}Si NMR spectrum (99.28 MHz) at 20 °C of NaOH/sorbitol tumbled with MPDMS for 12 months. 1180 repetitions. Recycle time = 10 s. Artificial linebroadening = 1 Hz.

(iii) Methoxy-terminated polydimethylsiloxane (MPDMS)

Methoxy-terminated PDMS tumbled in alkaline sorbitol for *12 months* yielded the same ^{29}Si resonances at –13, –21, and –44 ppm consistent with a tetraoxosilanol-sorbitol complex, an oligomeric D-centre, and a pentaoxosilanol-sorbitol complex. See Figure 3.12c. It appears that the possible pentaoxosilicon species is favoured by a longer period of degradation.

3.2 Quantification of Hydrolysis Products and Qualitative Rate Determination

A. Concentration of Hydrolysis Products

This study has so far shown that many silicones hydrolyse under many conditions to DMSD. However, the concentration of hydrolysis products is difficult to determine. Keenan *et al.* [42] have shown that inductively coupled plasma (ICP) analysis is unreliable when quantifying organosilicon compounds. Indeed, silicon concentrations determined by ICP in this study were clearly far higher than indicated by ^{29}Si NMR. We attempted to extract dissolved organosilicon compounds using a 1:1 mixture of methylisobutyl ketone and 1-pentanone [46] and ran ICP analysis on the organic phase. In principle, this would permit the quantification of both inorganic silicates and organosilicon compounds. However, the argon plasma could not be maintained when using this solvent system. In addition, silicon contamination from glass ICP components along with silicone adsorption on the sample delivery system made all attempts to utilize this method unsuccessful.

Ultimately a method based on ^{1}H NMR spectroscopy was devised. As discussed on page 13, the concentration data are presented in Table 3.2. Consistent with ^{29}Si NMR observations, the results indicate that the presence of an electron withdrawing end group on the silicone polymer makes the polymer more susceptible to hydrolysis. HPDMS consistently yielded higher concentrations of soluble degradation products than MPDMS, which in turn yielded more than PDMS.

Interestingly, both the implant silicones yielded a greater concentration of soluble decomposition products than PDMS.

The percent decomposition per year was obtained from the following expression:

$$\% \text{ decomp} = [Me_2Si \text{ mg } L^{-1} / \text{ total silicone mg per kg of solvent}] \times 100$$

where total silicone mg per kg of solvent is calculated from Table 2.2.

Table 3.2 Concentration of $(Me_2)Si$ groups of organosilicon compounds tumbled at 37 °C for varying lengths of time in aqueous systems [a].

Silicone	Medium	Duration	$[Me_2Si]$	% Decomp.	% Decomp. $year^{-1}$
HPDMS	NaOH	24 months	517	1.14	0.57
PDMS		24 months	28.2	0.058	0.029
MPDMS	NaOH-Sorbitol	12 months	612	0.50	0.50
HPDMS	Plasma	18 months	87.6	0.049	0.032
Silicone Shell		34 months	53	0.065	0.023
Silicone Gel		34 months	45	0.020	0.0070
HMDS		18 months	29.1	0.014	0.010
MPDMS		18 months	15	0.011	0.0073
PDMS		18 months	5.2	0.0022	0.0014
blank		18 months	0	0	0
HPDMS	Serum	18 months	78.1	0.033	0.022
MPDMS		18 months	14.8	0.0078	0.0052

[a] The samples correspond to those shown in Table 2.2.

B. Silicon detection limit using NMR Spectroscopy

The ^{29}Si DEPT-45 NMR spectrum of 0.064 mol kg^{-1} DMSD recorded over 4 hours consisted of two peaks with a total signal-to-noise ratio of approximately 170. Therefore, for a signal-to-noise ratio of 2, the DMSD concentration would need to be about 0.00075 mol kg^{-1}, corresponding to a detection limit of approximately 21 mg L^{-1} Si per spin site. Our detection limit is lower than that achieved by Keenan *et. al.* [42] using ^{29}Si NMR and over 17 hours of total acquisition, demonstrating the advantage in using ^{29}Si DEPT-45 NMR for the detection of hydrolysis products of silicone polymers.

Using ^{1}H NMR a much lower detection limit was achieved. A sample containing 517 mg L^{-1} Me_2Si groups had a signal-to-noise ratio of *ca.* 952 for the Me_2Si proton resonance after 13 minutes acquisition. See Figure 3.13. Therefore, a Me_2Si concentration of approximately 1.1 mg L^{-1} is necessary to have a signal-to-noise ratio of 2, corresponding to a Si detection limit of approximately 0.53 mg L^{-1} per spin site. The number of different Me_2Si-containing species does not affect their detection when using ^{1}H NMR because the methyl protons will resonate at nearly the same frequency in a wide variety of species. However, ^{1}H NMR does not give information regarding the nature of the species present in solution.

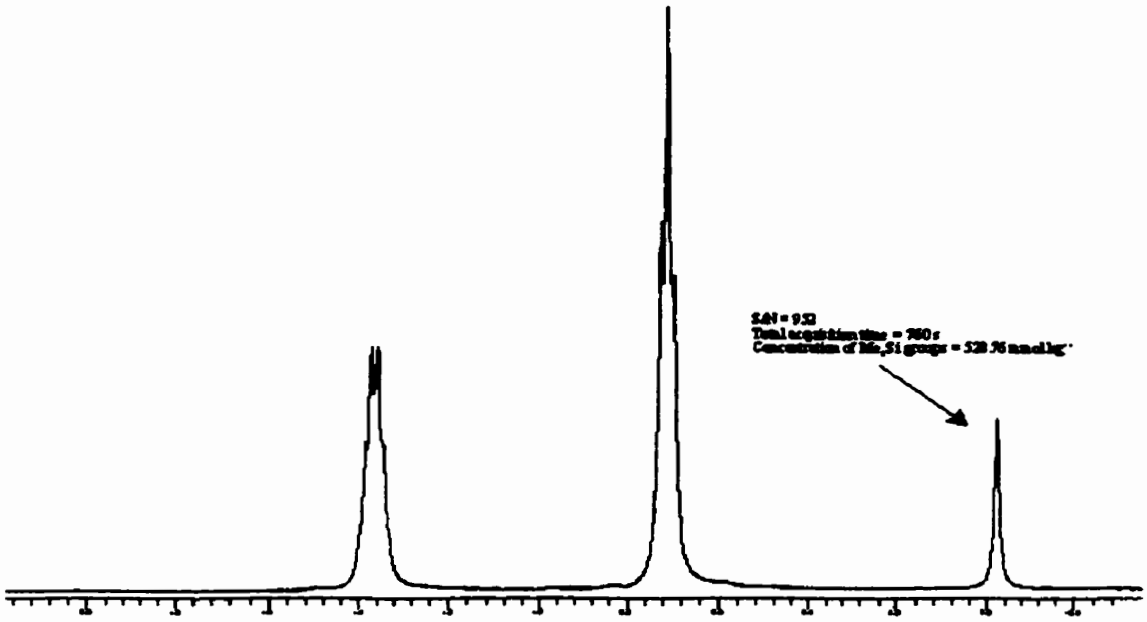


Figure 3.13 ^{1}H NMR spectrum (499.79 MHz) at 22 °C of 0.01 mol kg^{-1} NaOH tumbled with HPDMS. 64 repetitions. Recycle time = 10 s.

C. DMSD Equilibrium

The equilibrium between DMSD and its condensation products in DDW lies heavily towards DMSD. Silicon-29 NMR was used in an attempt to determine the equilibrium constant. Assuming that the activity coefficients of DMSD and TMDSD are both approximately one, then a plot of log[TMDSD] versus log[DMSD] should give a linear plot of slope 2 with a y intercept of log K.

$$\text{DMSD} + \text{DMSD} \rightleftharpoons \text{TMDSD} + \text{H}_2\text{O}$$

$$K = a_{\text{TMDSD}}\, a_{\text{H2O}} / a_{\text{DMSD}}^2$$

$$= a_{\text{TMDSD}} / a_{\text{DMSD}}^2$$

$$\log[\text{TMDSD}] = 2\log[\text{DMSD}] + \log K$$

DMSD was added in increasing amounts to water samples and the molarities of DMSD and TMDSD were determined by integration of the ^{29}Si NMR spectra. Figure 3.14 shows the log[TMDSD] *vs.* log[DMSD] plot along with linear regression analysis. The dashed line, representing the line of best fit, yielded an equilibrium constant of 0.313 ± 0.008 but with a slope of 1.2. When the slope is fixed at 2 (solid line), the resulting equilibrium constant is 0.560 ± 0.29.

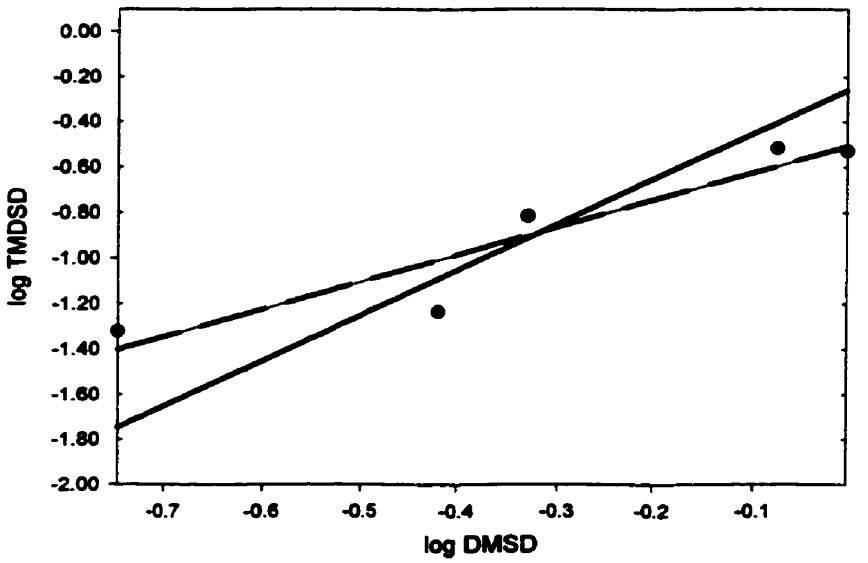


Figure 3.14 log[TMDSD] *vs.* lg[DMSD] plot. The dashed line represents the best fit described by the equation log[TMDSD] = -5.0 x 10^{-1} + 1.2log[DMSD]. The solid line represents the best fit when the slope is fixed at 2, described by the equation log[TMDSD] = -2.5 x 10^{-1} + 2log[DMSD].

3.3 Silicate-Polyol Complexes

The total Si concentration in a SiO_2 solution was observed to decrease upon addition of xylitol, as shown in Table 3.3. The implication here is that the Si-xylitolate complex is less soluble than SiO_2 at circum-neutral pH.

Table 3.3 Effect of xylitol on SiO_2 solubility at 37 °C.

Sample preparation	Si concentration (ppm)[a]
(a) SiO_2 saturated DDW, filtered [b] one week after silica addition (three trials)	71.8, 72.6, 74.2
(b) 0.87 mol kg^{-1} xylitol added to (a), tumbled for one week, then refiltered[b]	55
(c) 0.76 mol kg^{-1} xylitol added to SiO_2 saturated DDW in the presence of excess solid silica, filtered[b] after one week of tumbling	57.4

[a] Determined by ICP within two days of final filtration.
[b] Filtered using a 0.45 μm centrifuge filter. Third trial in (a) also filtered using 0.1 μm filter, with no apparent difference.

Meanwhile, the solubility data in Table 3.4 indicates that Si concentration decreases as sodium gluconate, another coordinating polyol, is increased even though the pH increases with gluconate concentration.

Table 3.4 SiO_2 solubility at 37 °C as a function of sodium gluconate concentration.[a]

Gluconate molality	pH	Si concentration [b] /mg L^{-1}
2.92	6.998	24.9
1.3	6.82	36.7
0.88	6.754	39.1
0.39	6.637	44
0.11	6.411	50.7

[a] Filtered using a 0.45 μm centrifuge filter. Tumbled for one week. [b] Determined by ICP.

Data in Table 3.5 indicates that, in solutions buffered to pH 7, coordinating polyols have no different effect on SiO_2 solubility than non-coordinating polyols. Table 3.6 shows that the simple addition of an electrolyte eliminates any differential influence polyols have on SiO_2 solubility. The implication here is that the drop in SiO_2 solubility caused by polyols (refer to Table 3.3) is associated with water structuring and a consequent decrease in water activity.

Table 3.5 SiO_2 solubility in various polyol solutions, buffered to pH 7.[a]

Polyol Solution	Si Concentration [b] /mg L^{-1}
0.056 M sodium gluconate	67.9
0.056 M sodium tartrate	66.6
0.055 M mannitol	67.4
0.065 M adonitol	66.9
none	68.2

[a] All media contained 0.029 M NaH_2PO_4 and 0.044 M Na_2HPO_4 in CO_2 and SiO_2 saturated DDW. [b] Determined by ICP.

Table 3.6 Effect of xylitol on SiO_2 solubility at 37 °C and constant ionic strength.

Sample Preparation[a]	Silicon Concentration /mg L^{-1}
solid SiO_2 added to water	56.9
solid SiO_2 added to 0.03 mol kg^{-1} xylitol	55.4
xylitol added to presaturated/filtered SiO_2 solution (0.03 mol kg^{-1} final xylitol concentration)	56.7, 57.3

[a] All media contained 1.01 mol kg^{-1} KNO_3 and were filtered (0.1 μm) prior to ICP analysis.

3.4 DMSD interaction with alkyl alcohols

As a consequence of using propanol for a concentration standard in the ^1H analysis of hydrolysis products, a remarkable observation was made. Figure 3.15 reveals that when propanol is added to a DMSD solution, a plethora of different species are formed. However, only DMSD, TMDSD, D_3 and D_4 may be assigned with any certainty. The down frequency shift of the remaining resonances, similar to that seen in alkoxy-substituted silicates species, indicates that, in all likelihood, they are from propoxy-substituted silanol species.

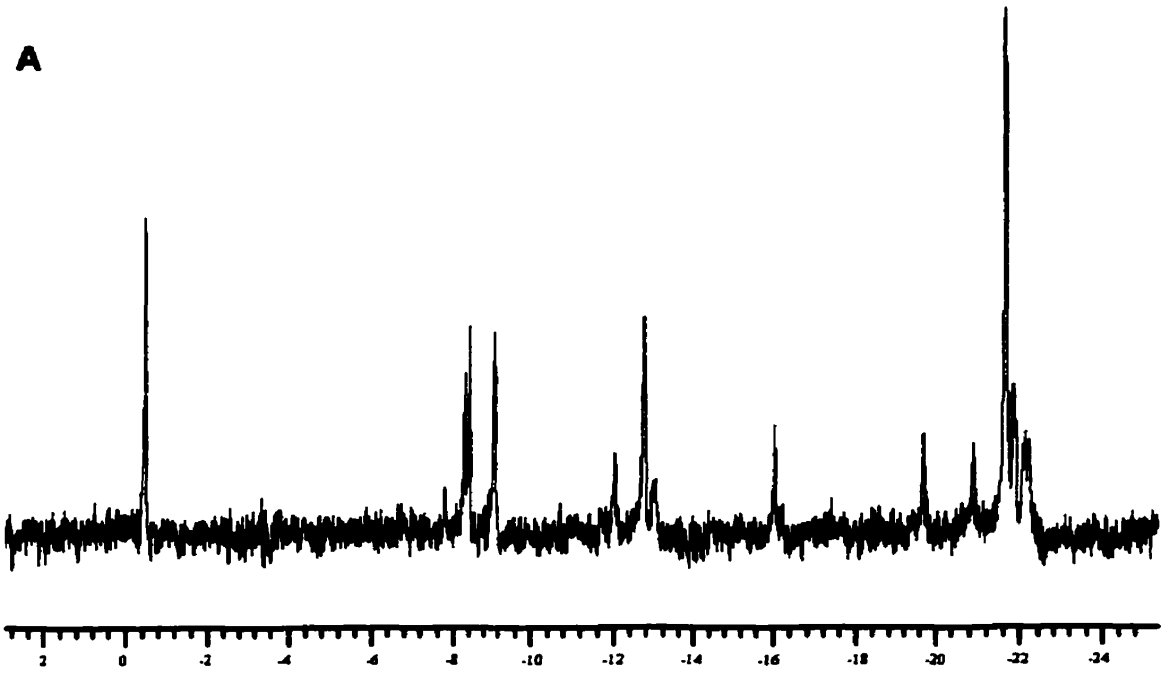


Figure 3.15 (A) DEPT-45 ^{29}Si NMR spectrum (99.28 MHz) at 22 °C of 0.004 M DMSD in 0.016 M propanol solution. 1300 repetitions. Recycle time = 10 s. Artificial linebroadening = 1 Hz.

3.5 DMSD-Carbohydrate Interaction

Silicon-29 NMR revealed no evidence that DMSD interacts directly at circum-neutral pH with aliphatic polyols known to complex aqueous silicate anions. Nonetheless, polyols increase the extent of DMSD dimerization, presumably because of a decrease in water activity. See Figure 3.16. The interaction between DMSD and various polyhydroxy alcohol species was investigated using ^{29}Si NMR. When DMSD is combined with xylitol, mannitol or inositol solution at pH 7, there is no evidence of an alkoxy linkage. The nature of the polyol species does not appear to affect the equilibrium between DMSD and TMDSD. Resonances consistent with DMSD and

TMDSD are observed at *ca.* –0.4 and –8.2 ppm respectively, with no evidence of further condensation reactions.

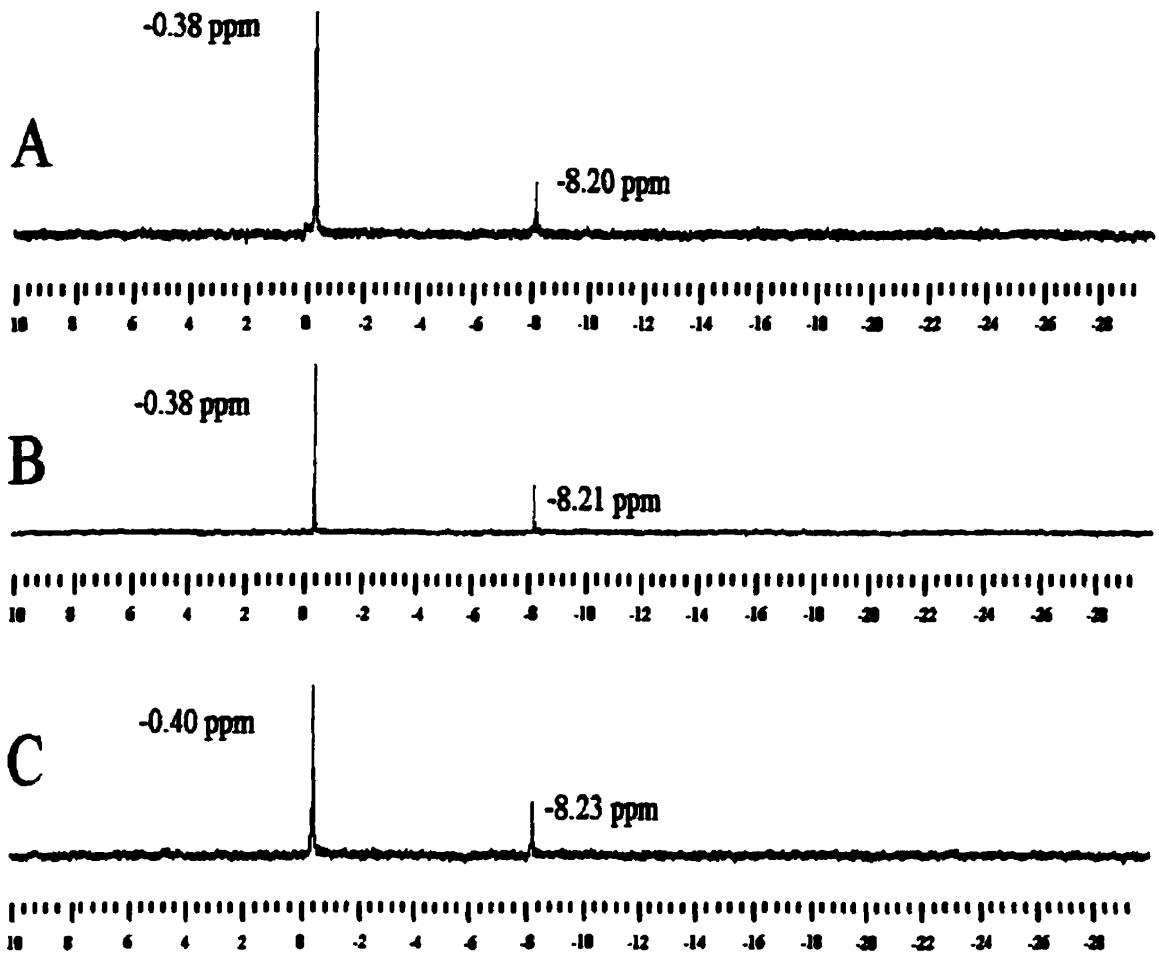


Figure 3.16 DEPT-45 ^{29}Si NMR spectra (99.28 MHz) at 23 °C of solutions containing (A) 0.415 mol kg^{-1} xylitol; (B) 0.44 mol kg^{-1} inositol; and (C) 0.435 m mannitol tumbled 1 day at 37 °C with DMSD (0.0627). Each spectrum was acquired with 1000-1300 pulse repetitions and a recycle time of 10 s. Artificial linebroadening = 1 Hz. The aliphatic polyols, xylitol and mannitol, are known to complex silicate anions in alkaline solution. Inositol does not. The resonances at -0.4 and -8.2 ppm correspond to DMSD and TMDSD, respectively.

Chapter 4-Discussion

4.1 Silicone Hydrolysis

A. Influence of the Aqueous Hydrolysis Medium

Significant amounts of water soluble silicon species were detected upon exposure to acid, base or blood plasma (pH 7.4). However, no evidence of hydrolysis was detected for any of the silicones after *2.5 months* exposure to either pure water or neutral aqueous sorbitol. Since these compounds were not detected in the pure water or aqueous sorbitol media they appear to be true decomposition products and not merely impurities released from the silicone polymers. In addition, DEPT-45 ^{29}Si NMR analysis of the silicone polymers reveals that there are no impurities present. It is apparent, therefore, that silicone hydrolysis is catalysed by acids, bases and one or more dissolved components of blood.

Interestingly, the rate of hydrolysis for HPDMS and MPDMS is about 1.4 times greater in plasma than serum. In human blood plasma the ratio of reaction rates for HPDMS:MPDMS:PDMS is approximately 22:5:1. However, in 0.1 M NaOH the HPDMS:PDMS reactivity ratio is only 5:1. This implies that the terminal group plays a more important role than in silicone hydrolysis in blood plasma.

B. Influence of the Polymer Chain's Terminal Substituent

The extent of silicone hydrolysis consistently increased with the electron withdrawing ability of the substituent terminating the polymer chain. For a given set

of reaction conditions, the concentration of hydrolysis products increased as HPDMS > MPDMS > PDMS. These observations suggest that silicone hydrolysis occurs primarily via end group (-$OSiMe_2R$) scission.

In organic chemistry, acid or base promoted hydrolysis reactions are well known, proceeding through a nucleophilic substitution mechanism [47]. In base catalyzed hydrolysis, an electrophilic carbon acts as a reaction site for nucleophilic attack. Silicon is much more electrophilic than carbon and, thus, more prone to undergo hydrolysis reactions. For example, R_3Si-X (where X is a halogen) hydrolyzes far more rapidly than R_3C-X. In the proposed base catalyzed hydrolysis mechanism shown in Figure 4.1, a hydroxide ion (nucleophile) bonds with the end group's silicon atom (electrophile), causing the siloxane bond to cleave.

In general, acid-catalyzed hydrolysis of organic molecules is initiated by protonation of an electron dense species, *i.e.*, oxygen [47]. The protonated oxygen makes the attached carbon more electrophilic and, thus, more prone to hydrolysis. In silicones, the siloxane bridging oxygens would have similar electron densities and, therefore, protonation may occur at any of these oxygen atoms. See Figure 4.2. The random protonation of the siloxane bridging oxygens would mean that the terminal substituent on the polymer chain does not play as crucial a role as in the base catalysed mechanism.

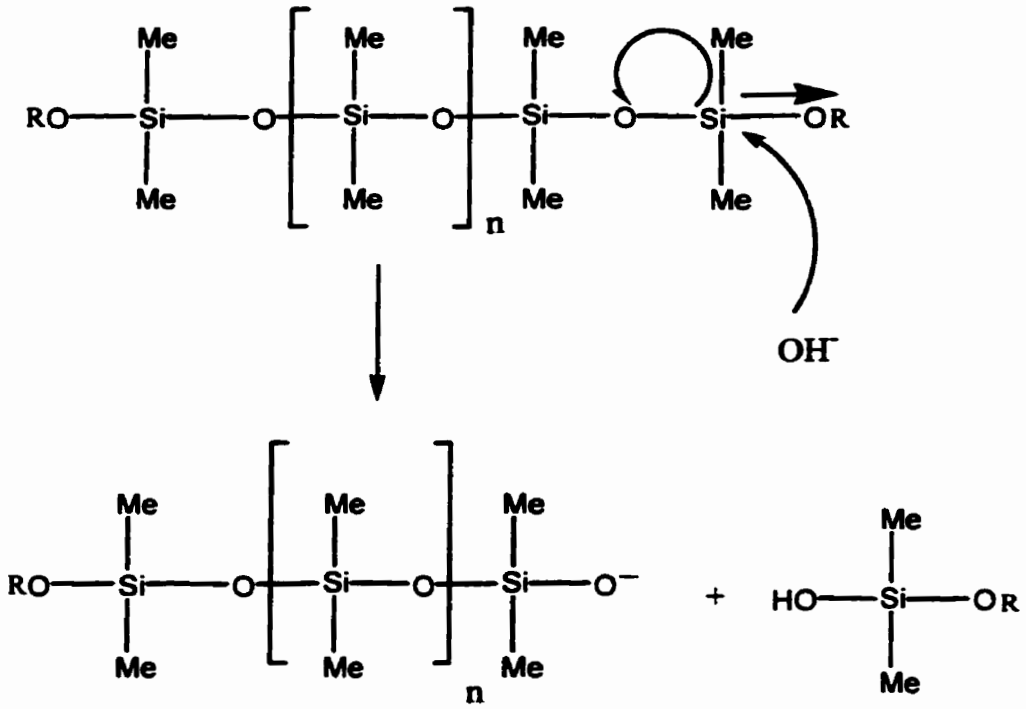


Figure 4.1 Proposed base catalyzed silicone hydrolysis mechanism where R = H or Me.

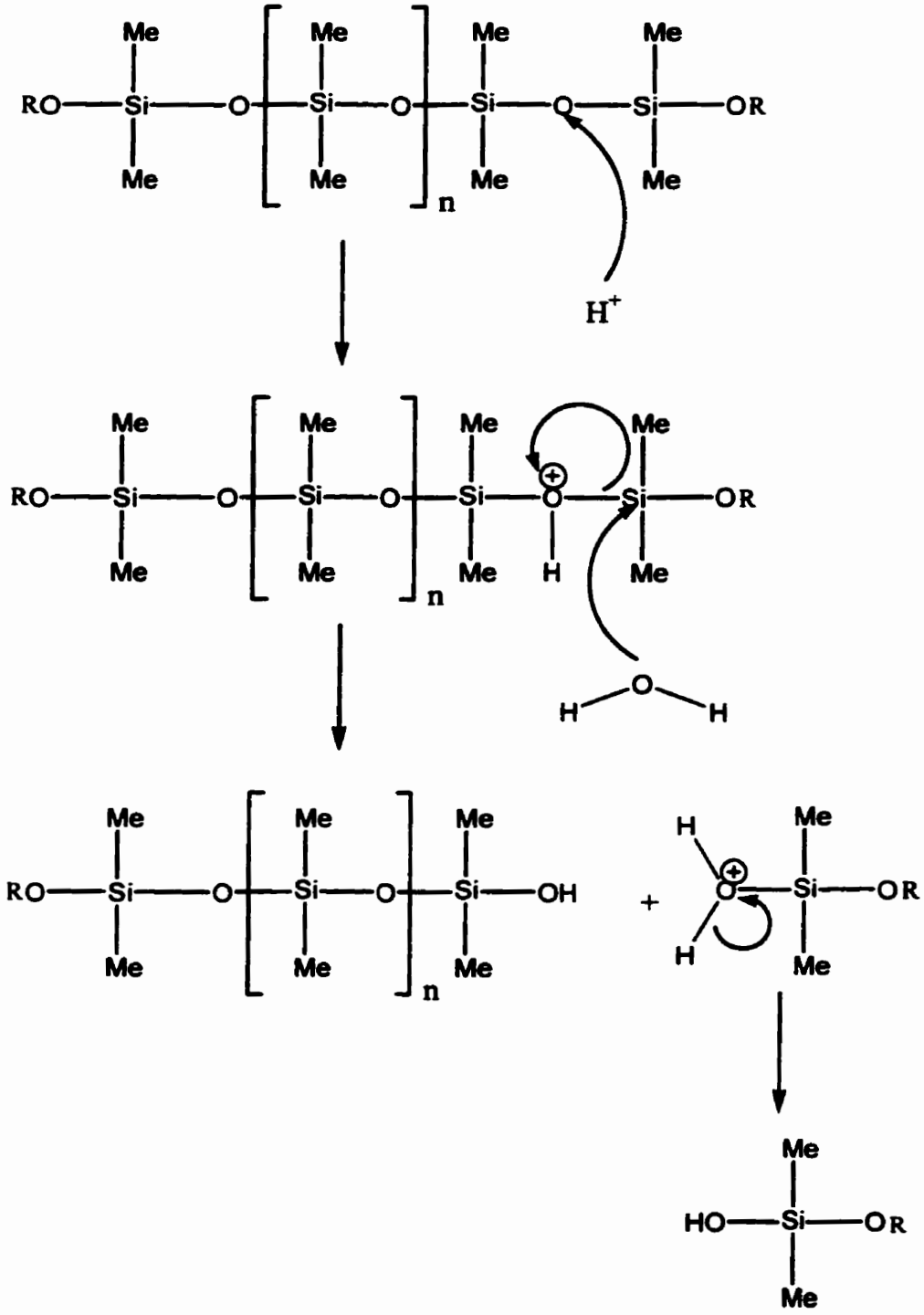


Figure 4.2 Acid catalyzed hydrolysis of methyl–silicone where R = H or Me.

The catalytically active species in human blood plasma is not known. Human blood has many constituents, making it impossible here to ascertain the catalytically active species facilitating silicone hydrolysis.

PDMS undergoes hydrolysis to DMSD just as in the case of substituted silicones, but much less readily. It appears that the terminal groups on the silicone polymer are the reactive starting points for hydrolysis, which then progresses down the chain. In some cases, however, the reactive end can fold back over the chain causing cyclization (refer to Figure 4.3). The generation of the reactive end group is an essential step in silicone hydrolysis. This occurs less readily in MPDMS and especially in PDMS, the -Me group being much less reactive.

Hexamethyldisiloxane also underwent hydrolysis to DMSD like the other silicones investigated. However, HMDS hydrolysis can not proceed through the mechanisms proposed above since it contains neither an electron withdrawing end group (Figure 4.1 or 4.2), nor enough siloxane linkages to form cyclic intermediate species (Figure 4.3). Moreover, HMDS was the only silicone to undergo methyl cleavage to form silicic acid in human blood plasma. There was no indication by ^{29}Si NMR that the HMDS was contaminated, and identical findings were obtained using different sources of both HMDS and blood. It seems clear, therefore, that HMDS undergoes hydrolysis via quite different mechanisms than any of those proposed above. Once hydrolysis occurs, it is well on its way to forming silicic acid.

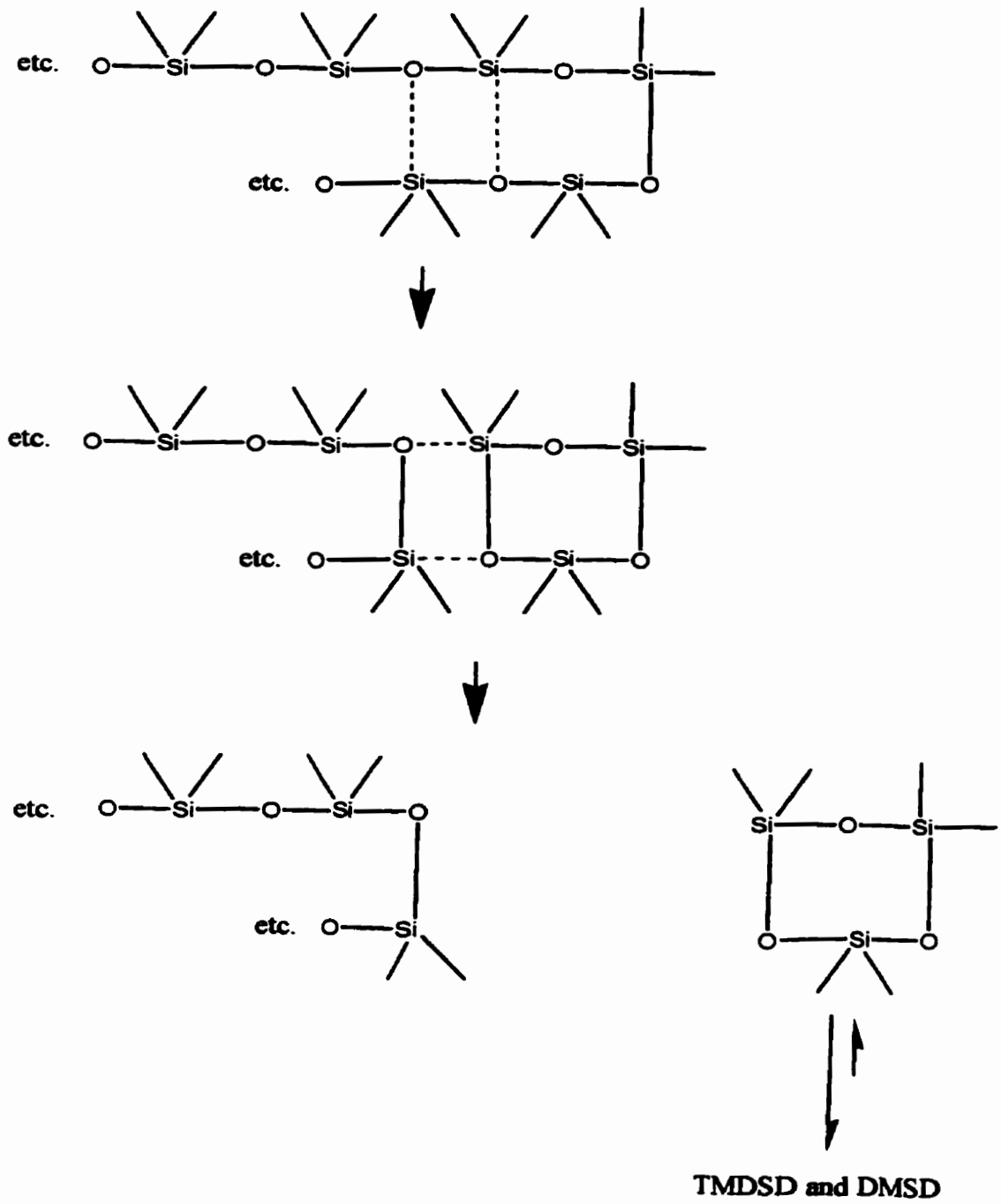


Figure 4.3 Hydrolysis of silicone to DMSD via intramolecular cyclization reaction.

4.2 Chemistry of Hydrolysis Products

A. Speciation of Hydrolysis Products

There have been several published reports indicating that DMSD is the primary water soluble hydrolysis product of PDMS on soil [23, 30-31]. However, only two papers report ^{29}Si NMR spectroscopy data of DMSD in aqueous systems [21,42]. Moreover, the solution conditions must be clearly defined since the solvent composition will cause significant variation in the ^{29}Si chemical shifts of methyl silane compounds, precluding the direct comparison of chemical shift from previous reports [43]. In the present study we compared the chemical shifts of ^{29}Si resonances resulting from silicone degradation with those we measured for potential hydrolysis products (*i.e.*, DMSD, TMDSD, D_3 and D_4 dissolved in water). When pure DMSD was added to water and analysed by ^{29}Si NMR spectroscopy, a chemical shift very similar to that of the principal hydrolysis product was observed (*i.e.*, about −1 ppm). None of the other potential hydrolysis products, *i.e.*, D_3 and D_4, had chemical shifts near that of the resonances resulting from silicone depolymerization. Therefore, it is most likely that the primary hydrolysis product of silicone depolymerization in an aqueous environment is DMSD. In addition, when the concentration of DMSD in water is increased, a second resonance from TMDSD at *ca.* −8 ppm is detected. The difference in chemical shift between DMSD and TMDSD is very similar to that observed in figure 3.3b. Therefore, the only other hydrolysis product that can be assigned with certainty is TMDSD.

It would be expected that a longer period of decomposition would result in higher concentrations of DMSD. However, in many cases a resonance at –23 ppm consistent with D-units from a silicone oligomer was observed (see Figures 3.2a, 3.8b, 3.9b, 3.10b, 3.11b). The D-centre resonance is unaffected by filtration and therefore associated with a low molecular weight, water-soluble oligomer. Since it yields just a single D resonance, the species is almost certainly a symmetrical ring structure. In addition, with the exception of D_5 and D_6 (see Table 3.1), there are no other possible symmetrical structures in the literature with similar chemical shifts. However, at the Me_2Si concentrations where it is observed, DMSD should be the only water soluble silicon containing hydrolysis product, precluding the possibility of larger ring sturctures. Without further investigation it is impossible to assign the species responsible for the D-centre resonance.

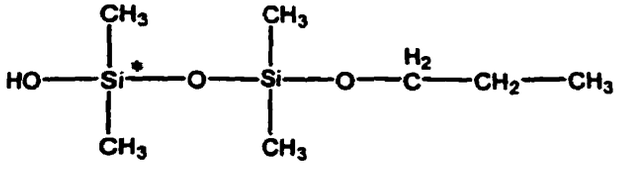
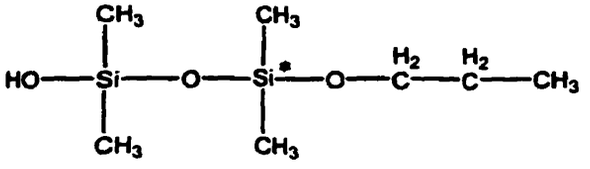
Of the possible hydrolysis products, only DMSD and TMDSD have significant water solubility. It was determined that DMSD is highly favoured over TMDSD, the equilibrium constant for dimerization being 0.56 ± 0.29. Accordingly, should larger oligomeric species result from hydrolysis, they would in all likelihood be converted to DMSD.

B. Interaction of Hydrolysis Products with Organic Alcohols

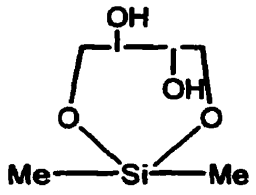
Silicates are known to condense with mono- and polyhydroxy alcohols to form alkoxy-substituted silicate species [10,11]. It seems feasible that DMSD and TMDSD

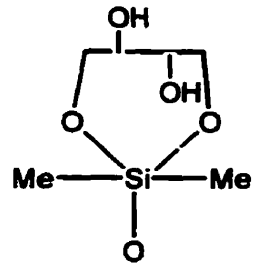
could behave similarly. Indeed, the formation of alkoxy-substituted silanol species was observed when DMSD was combined with a propanol solution, resulting in a plethora of ^{29}Si NMR signals. The resonances at –0.51, –7.83, –9.1 and –19.75 ppm are consistent with DMSD, TMDSD, D_3 and D_4 respectively. When silicates condense with methanol or ethanol, there is a *ca.* –0.5 ppm shift difference between the alkoxy-substituted and non-substituted silicon resonances [10]. Therefore, it seems likely that the resonances at –8.32 and –8.45 ppm may be from a propoxy-TMDSD species (See Table 4.1). However, the remaining resonance can not be assigned at this time. In addition, propanol has a much greater affinity for DMSD (or TMDSD) than for silicates, which may be due to the increased hydrophobic character of DMSD compared to silicates.

Table 4.1 Proposed structures for silanol species interacting with R = propyl.

Si Chemical Shift	Structure
–0.51	DMSD
–7.83	TMDSD
–8.32	
–8.45	
–9.1	D_3
–12.04	?
–12.76	?
–13.06	?
–16.06	?
–19.75	D_4
–20 to –23	D units in oligomer

When the silicone polymers investigated were tumbled in a highly alkaline sorbitol solution, two new signals at *ca.* –13 and –44 ppm were observed in the ^{29}Si NMR spectra. Silicates are known to condense with sorbitol under alkaline conditions [12]. Therefore, it would seem likely that the resonance at *ca.* –13 ppm is from a tetraoxo dimethylsilanol-sorbitol complex. It is also known that a change in coordination number of silicon results in a *ca.* 30 ppm down frequency shift of the corresponding ^{29}Si resonance. Therefore, the signal at –44 ppm may be from a pentaoxo dimethylsilanol-sorbitol complex. See Figure 4.5.





tetraoxo dimethyl-sorbitol complex pentaoxo dimethyl-sorbitol complex

Figure 4.5 Proposed tetra and pentaoxo dimethylsilanol-sorbitol complexes.

Alternatively, the signal at *ca.* –44 ppm may be from trioxo-methylsilane. $MeSi(OR)_{3-n}(OH)_n$, where R is an alkyl group, will resonate around –40 ppm in the ^{29}Si spectrum. See Table 3.1. It is conceivable that a compound such as this may be formed with sorbitol, however, it would require bonding not previously seen with silicates. Further investigation is required to assign these resonances with any certainty.

Conclusions

We determined for the first time that methyl silicones undergo hydrolysis in dilute acids, bases and human blood plasma–without mineral or biological mediation. Similar hydrolysis products are not observed in pure water, aqueous sorbital, or the parent silicone polymers indicating that water soluble silicon species are not leached

out of the silicone polymer, and thereby providing additional evidence that decomposition has occurred. The rate of hydrolysis is significantly higher for polymers containing electron-withdrawing hydroxy or methoxy end groups, with the rate increasing as PDMS < MPDMS < HPDMS. The shell and interior of a silicone mammary prosthesis exhibited intermediate rates of hydrolysis, indicating the presence of a significant level of electron-withdrawing end groups. If the rate of hydrolysis has zeroth-order dependence then approximately 1% of the silicone shell will decompose in 100 years. This is based on a 3x3 cm square of silicone shell being cut into 100 3x3 mm squares having a surface area of 23.16 cm^2 and weighing 0.3985 g. Therefore, the 0.0023 g of Me_2Si per gram of shell translates to about 3.923 μg per cm^2 of shell. If one assumes a 500 mL spherical shell with a radius of 4.916 cm, 1.19 mg of the shell would decompose per year. In other words, the shell degrades, but not rapidly. However, this is extrapolated from limited amounts of data.

The initial water-soluble hydrolysis product is dimethylsilanediol; however, after prolonged degradation, a highly symmetrical oligomer (with, as yet, unknown structure) eventually dominates the aqueous medium. Hexamethyldisiloxane additionally yields silicic acid upon hydrolysis in human blood plasma, suggesting that silicates are the ultimate degradative fate of silicone in the body. In addition, dimethylsilanediol condenses with propanol in alkaline solutions to yield a wide variety of species.

DEPT-45 ^{29}Si NMR proved very useful for detecting the various silicone hydrolysis products at reasonably low concentrations. Proton NMR is a more reliable method for determining the total concentration of aqueous silicones than ICP, the detection limit being at the sub ppm level after ca. 15 min acquisition.

Future Work

Silicone Hydrolysis

The end group on silicones has a profound influence on the stability of the polymer. The presence of an electron withdrawing end group causes the silicone to undergo hydrolysis much more readily. To increase the stability of the silicone new capping procedures should be investigated. Possible solutions may include different capping agents or a more efficient method of trimethylsilation.

It is obvious that silicone medical implants are exposed to a significant amount of blood. However, the catalytically active species in the hydrolysis of silicones in human blood plasma is not yet known. It is important to ascertain this species so as to make a silicone that is more resistant to hydrolysis in the body.

Silicone interaction with alcohols and carbohydrates

Silanols present as hydrolysis products of silicones have a high affinity for alcoholic species in solution. There are many biologically relevant molecules, such as carbohydrates, that contain hydroxy groups which may condense with silanol groups. An extensive library of silanol-complexing aliphatic alcohols and carbohydrates can

be made with relative ease using ^{29}Si DEPT NMR. In addition other NMR techniques such as ^{13}C, ^{1}H and INEPT can be used to gain structural information to assign structures to new resonances, *i.e.*, signals at *ca.* –13 and –44 ppm in Figure 3.12.

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