Synthesis and Characterization of Polysiloxanes for Controlled Release of 2-Pyridine Aldoxime–Chloride

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ABSTRACT: A number of polysiloxanes and their copolymers were synthesized by hydrolytic polycondensation of dialkyl (ary) dichlorosilane or their mixtures in a saturated solution of NaCl in water at low temperature (0–5°C). These polysiloxanes were characterized by intrinsic viscosity, infrared and nuclear magnetic resonance spectroscopy. 2-Pyridine aldoxime–chloride (PAM–Cl) was incorporated into these polysiloxanes, followed by crosslinking with tetraethoxysilane using dibutyltindilaurate as catalyst. The effect of pH on *in vitro* release rate of PAM–Cl from polysiloxane matrices was investigated in phosphate buffer of pH 3.0, 7.4, and 10.0 at 37°C using an ultraviolet spectrophotometer. Transport parameters like the order of release and diffusion coefficients for these systems (polysiloxane—PAM–Cl) were also calculated. © 1998 John Wiley & Sons, Inc. J Appl Polym Sci 70: 1837–1846, 1998

Key words: polysiloxanes; controlled release; biocompatiblity; physiologically inert diffusion coefficients; transport parameters

INTRODUCTION

Silicone elastomers have long been known for their exceptional ability to exhibit and retain mechanical properties over a broad temperature range. The main interest in these materials stems from the fact that they possess unique properties, such as good low-temperature flexibility, excellent electrical properties, water repellency, and chemical and physiological inertness combined with biocompatibility not common in hydrocarbon polymer.[1] Due to its outstanding properties, the poly(dimethylsiloxane) (PDMS) elastomer has established itself as a well-known biomaterial and it has had a long history of biomedical applications.[2–5] Presently, silicone elastomers have become indispensable part for many controlled drug delivery systems. The suitability of this system for controlled release coating is primarily dependent on the permeability of silicones to various drug molecules.[6–10] PDMS is popularly used to manufacture marketable devices for long-term administration of steroidal drugs. In the past decade, much effort has been made to demonstrate that monolithic matrices based on this material are opt to release water soluble drugs and proteins at controlled rates.[11,12] The research was focused on prolonged release systems with a potential to be implanted or inserted into body cavities. Further, the prospect of developing PDMS-based controlled release matrices for oral use has raised interest.[13,14] *In vitro* drug release of number of drugs, that is, chloropheniramine maleate, pseudoepherdrine hydrochloride, dextromethorphan hydrobromide, papaverine hydrochloride, clonidinehydrochloride, and salicylamide have

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been studied for oral applications using PDMS as a matrix material. The reported literature suggested that controlled release rate studies have been carried out using only PDMS as a matrix materials. We have already reported the efficacy of polysiloxanes[15] as matrix materials for slow release of PAM–Cl, an antidote against organophosphorous poisoning. The effect of viscosity of polysiloxane matrices on *in vitro* release rate of PAM–Cl and the time taken for 80% PAM–Cl release was also studied. We are therefore reporting the synthesis and characterization of polysiloxanes for controlled release of 2-pyridine aldoxime–chloride (PAM–Cl). The effect of pH on the *in vitro* release rate of PAM–Cl has also been reported in the present article.

EXPERIMENTAL

Chemicals required for the present study, that is, dimethyldichlorosilane, vinyl methyl dichlorosilane, diethyl dichlorosilane, diphenyl dichlorosilane, tetra-ethoxy silane, and dibutyl tin dilaurate were procured from M/s Fluka and used as received. 2-Pyridine aldoxime-iodide was procured from M/s Troika Parentalis Ahmedabad (India).

Synthesis of Polysiloxanes

Linear polysiloxaediols were prepared by controlled hydrolysis of dichlorosilanes or mixture of dichlorosilanes using satured solution of sodiumchloride in water in 1 : 2 ratio (V/V) at 0.5°C over a period of 2 h.[15,16] The reaction mixture was kept at room temperature for about 24 h, extracted with ether and dried over anhydrous sodiumsulphate. A number of polysiloxanes, that is, PDMS, Poly(vinyl methyl siloxane) (PVMS), Poly(diethylsiloxane) (PDES), and copolymers of the abovementioned polysiloxanes were synthesized for the present study.

Synthesis of 2-PAM–Cl

2-PAM–iodide was treated with methanolic hydrochloride to get 2-PAM–Cl and purified by recrystallization with ethanol, as reported in the literature.[17]

Characterization

These polysiloxanes were characterized by viscosity, infrared (IR) and nuclear magnetic resonance (NMR) spectroscopy. Intrinsic viscosity of these polymers was determined in toluene at 30 ± 1°C using an ubbelohde viscometer. Fourier transform infrared (FTIR) spectra were recorded in the 400–4000 cm^{-1} range using a Perkin–Elmer FTIR-1720X spectrometer. NMR spectra of polysiloxanes were recorded in deuterated benzene at 90MHz (Jeol-Japan) using tetramethyl silane as an internal standard.

Curing of Polysiloxanes

Mixture of tetraethoxysilane and dibutyltindilaurate in a ratio of 3 : 1 was prepared by weighing and mixing these chemicals accurately. 10 g of unfilled polysiloxane was weighed, and 2–3% catalyst mixture was added. This mixture was poured over the aluminium tray (18.5 × 23 in.). Curing was done at room temperature in air over a period of 20–40 h. These polysiloxanes were converted into crosslinked membranes.

Drug Incorporation in the Polymer Matrix

2-PAM–Cl was incorporated in each polysiloxane matrix by the bulk method,[15] that is, addition of PAM–Cl before addition of curing agents. 20% PAM–Cl was blended with each of polysiloxanes and mixed properly. The mixture is cured at room temperature in the presence of 2% crosslinking mixture (TES + DBTL).

In Vitro Drug (PAM–Cl) Release Measurements

For the study of *in vitro* drug release under various pH conditions, the drug loaded polysiloxane was placed in 250-mL phosphate buffer of pH 3.0, 7.4, and 10.0 at 37°C under unstirred condition. The release of PAM–Cl in the medium was determined[18,19] by taking out an aliquot portion (0.1 mL) of it at suitable time intervals and measuring its absorbance after suitable dilution in 0.1*N* NaOH at λ_{max} 336 nm using a Shimadzu ultraviolet (UV) spectrometer.

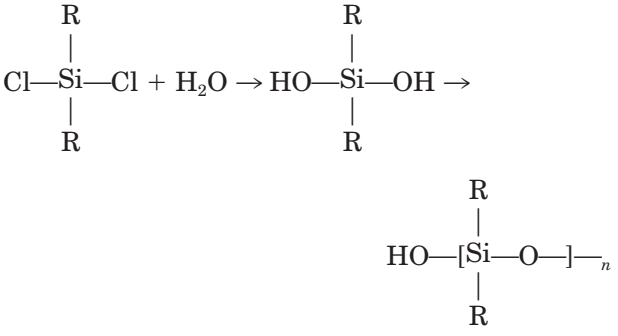
RESULTS AND DISCUSSION

The synthesis of polymeric organosiloxanes was first reported by Kipping[20] and his coworkers using hydrolysis of disubstituted silicon chlorides,

Table I Polysiloxanes Synthesized for the Present Study with Respective Intrinsic Viscosities in Toluene at 30°C

Sr. No.	Polysiloxane	Intrinsic Viscosity (dL/g)
1	Polydimethyl siloxane	0.25
2	Poly(vinyl methyl siloxane)	0.17
3	Poly(diethyl siloxane)	0.09
4	Poly(dimethyl-vinylmethyl) siloxane[a]	0.21
5	Poly(dimethyl-diethyl) siloxane[a]	0.16
6	Poly(vinylmethyl-diethyl) siloxane[a]	0.13
7	Poly(dimethyl-diphenyl) siloxane[a]	1.08
8	Poly(vinylmethyl-diphenyl) siloxane[a]	0.06

[a] Composition = 75 : 25.



Patnode[21] exploited the preparation of dimethylsilicones from dimethyldichlorosilane with or without the cohydrolysis with trimethylchlorosilane. Hydrolysis of dimethyldichlosilane in the presence of strong acids, alkaline conditions, alcohol, and carboxylic acids was reported to give polydimethylsiloxanes of high molecular weight. Since then, a number of methods have been reported for synthesis.[22] We have preferred hydrolysis in presence of salt hydrates[18] to get polymers of higher molecular weights and higher purity levels. This is one of the simplest methods, and reaction conditions are not very difficult. Impurities and acid evolved in the process remain in the aqueous phase and are easily removed.

Polysiloxanes synthesized by hydrolytic polycondensation have been given in Table I, along with their respective intrinsic viscosities (η) in toluene at 30°C. PDMS has (η) of 0.25 dL/g. Intrinsic viscosity of polyvinylmethylsiloxane (PVMS) reduced to 0.17 dL/g. The change in viscosity of PVMS may be explained due to replacement of 1 methyl group by a vinyl group in dimethyldichlorosilane, which might have reduced the hydrolysis rate during synthesis, resulting in PVMS of reduced viscosity. Viscosity of PDES is further reduced to 0.09 dL/g. Further hydrolysis of diphenyl dichlorosilane led to the formation of diphenylsilane diol of viscosity 0.02 dL/g.

Polysiloxane copolymers, that is, poly(dimethylmethylvinyl) siloxane P(DM-VM)S, poly(dimethyl-diethyl) siloxane P(DM-DE)S, poly(vinylmethyl-diethyl) siloxane P(VM-DE)S, poly(dimethyl-diphenyl) siloxane P(DM-DP)S, and poly(vinylmethyl-diphenyl) siloxane P(VM-DP)S synthesized under identical hydrolytic conditions were having intrinsic viscosities of 0.06–0.21 dL/g, intermediate to the values corresponding to the homopolymers.

Infrared Spectra

Polysiloxanes synthesized in the present study have also been characterized by FTIR. The FTIR spectra of PDMS show a strong peak at 1080 cm^{-1} and a shoulder peak at 1000 cm^{-1} due to Si—O—Si bond, indicating the formation of siloxane polymers. Strong bands at 1260 and 804 cm^{-1} may be due to dimethyl groups attached to silicon atom [—$Si(CH_3)_2$]. Strong peaks at 2960 and 1413 cm^{-1} due to νC—H and δC—H have also been observed in FTIR spectra of PDMS.

FTIR spectra of PVMS also show a strong peak at 1110 cm^{-1} due to Si—O—Si bond. Strong band at 1262 cm^{-1}, along with peaks at 798 cm^{-1}, indicated the presence of CH_3 and vinyl groups attached to silicon (CH_3—Si—CH═CH_2). Vinyl group is also indicated by the presence of νC═C at 1600 cm^{-1}.

Similarly, FTIR spectra of PDES show sharp peaks at 1010–1100 cm^{-1} showing the presence of Si—O—Si bond. Sharp peaks at 1250 and at

Table II *In Vitro* Release Rate Kinetics of 2-PAM–Cl from Polysiloxane Matrices at PH 7.4 and 37°C

Time (h)	% Release of 2-PAM–Cl from Polysiloxane Matrices				
	PDMS	PVMS	P(DM-VM)S (75 : 25)	P(DM-DE)S (75 : 25)	P(VM-DE)S (75 : 25)
$\frac{1}{2}$	27	26	21	29	30
1	34	35	27	38	39
2	42	45	35	49	51
3	48	54	40	58	62
4	53	60	45	66	71
5	57	66	51	73	80
6	60	72	58	78	—
7	63	79	62	—	—
8	66	82	67	—	—
9	69	—	72	—	—
10	72	—	79	—	—
11	74	—	—	—	—
12	76	—	—	—	—
13	78	—	—	—	—
14	80	—	—	—	—

750 cm^{-1} indicate that Si is attached to diethyl group [C_2H_5)Si]. Peaks at 2900 and 2979 cm^{-1} may be due to νC—H of ethyl group attached to silicon.

FTIR spectra of polysiloxane copolymers were also analyzed. Polysiloxane copolymers, that is, P(DM-VM)S, P(DM-DE)S, P(VM-DE)S, P(DM-DP)S, and P(VM-DP)S, show sharp peaks at 1000–1100 cm^{-1} due to Si—O—Si bond. Peaks at 1260–1262 cm^{-1} and at 798–803 cm^{-1} may be due to Si—C in copolymers P(DM-VM)S, P(DM-DE)S, and P(VM-DE)S. All these copolymers are showing peaks at 2962 and 1414–1468 cm^{-1} due to νC—H and δC—H vibrations. In the case of a phenyl ring containing siloxane copolymers, C—H stretching vibrations shifted to 3053–3071 and 700 cm^{-1} due to aromatic ring, as indicated in FTIR spectra of P(DM-DP)S and P(VM-DP)S copolymers. However, an Si—O—Si band was observed at 1000–1100 cm^{-1} in these copolymers.

In all these spectra, there was no peak at 666 cm^{-1} due to Si—Cl, confirming the formation of Si—O—Si bond during hydrolysis. Further presence of Si—O—Si, Si—C, and C—H peaks in FTIR spectra of polysiloxanes is in confirmity with the reported literature.[23]

Nuclear Magnetic Resonance Spectroscopy

NMR spectra were recorded in deuterated benzene at 90 MHz. NMR spectra further supports the results of IR spectra of polysiloxanes. The NMR spectra of PDMS a show characteristic peak due to methyl protons (CH_3—Si) at δ0.3 ppm (Singlet).

Further, in the NMR spectra of PVMS, there is a singlet at δ0.3–0.5 ppm corresponding to characteristic peaks due to methyl protons (CH_3—Si) and a multiplet in the range of δ5.7–6.4 ppm corresponding to vinyl protons.

In NMR spectra of PDES, there is a triplet in the range of δ0.4–0.9 ppm and a quardret in the range of δ1.0–1.4 ppm corresponding to CH_3 and CH_2 groups of ethyl group attached to a silicon atom (CH_3CH_2—Si).

In the NMR spectra of P(DM-VM)S copolymers, a singlet at δ0.3 ppm corresponding to methyl protons and a multiplet in the range δ5.0–6.2 corresponding to the vinyl group were observed, indicating the formation of poly (dimethyl-*co*-vinyl methyl siloxane).

Similarly, in the P(DM-DE)S siloxane copolymer, a singlet at δ0.1–0.4 ppm confirms the presence of methyl protons. Further, a triplet and quardret at δ0.4–0.9 and δ0.9–1.3 ppm, respectively, confirms the presence of C_2H_5 and CH_3 groups attached to a silicon atom (C_2H_5—Si and CH_3—Si) in the P(DM-DE)S copolymer.

P(VM-DE)S was characterized by a triplet and quardret at δ0.4–0.9 and δ1.0–1.4, respectively, corresponding to the ethyl group and a multiplet at δ5.5–6.2 ppm corresponding to the vinyl group.

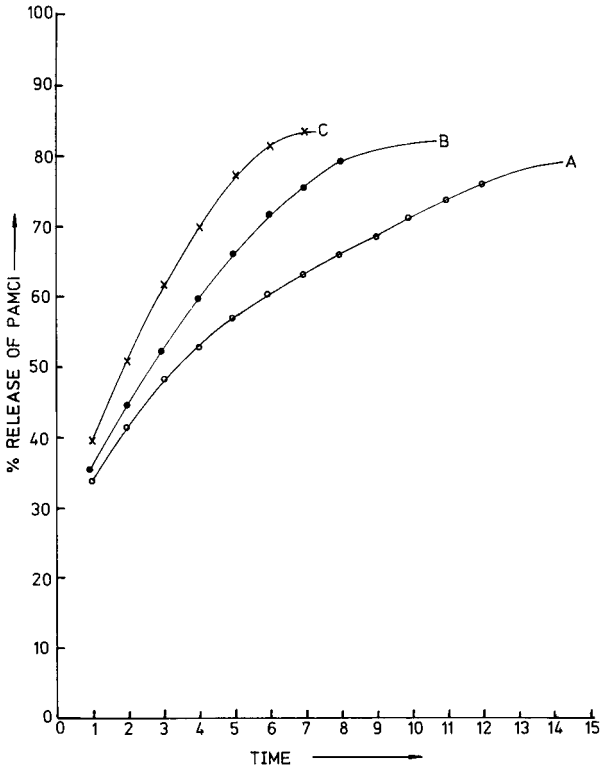


Figure 1 Plot of the percentage of PAM–Cl released versus time for (A) PDMS, (B) PVMS, and (C) P(VM-DE)S at pH 7.4.

Copolymers of P(DM-DP)S and P(VM-DP)S and their formation are evident by the presence of a multiplet in the range of δ7.2–8.1 ppm due to phenyl protons, in addition to a peak at δ0.1–0.4 ppm due to CH_3—Si in the NMR spectra of P(DM-DP)S. In the case of the P(VM-DP)S copolymer, a multiplet due to phenyl protons shift to δ6.6–8.2 ppm. Other peaks due to vinyl protons shift to δ5.7–6.4 ppm and methyl protons of CH_3—Si at δ0.1–0.4 ppm, respectively. The multiplet at δ6.6–8.2 ppm indicates the mixing of resonance frequencies of —CH═CH_2 and a phenyl ring. Due to the closeness of resonance frequencies, separate peaks due to phenyl and vinyl groups could not be realized. However, the presence of these groups is evident in their respective IR spectra.

In Vitro PAM–Cl Release

We have already reported the release of PAM–Cl from PAM–Cl-loaded PDMS matrix in a phosphate buffer of pH 7.4 at 37°C. It was observed that PDMS[15] of [η] equal to 0.25 dL/g does not release PAM–Cl, whereas PDMS of [η] equal to 0.10 dL/g releases PAM–Cl very quickly (95% drug release in 1 h). Assuming that there was similar level of crosslinks in the systems, release of PAM–Cl from a PDMS matrix is viscosity-dependent. Therefore, we have selected an intermediate viscosity of [η] = 0.18 dL/g to prepare polysiloxane matrices for controlled release of PAM–Cl. Keeping this parameter constant [(η) = 0.18 dL/g], other polysiloxane matrices of similar viscosities were investigated for PAM–Cl release at pH 3.0, 7.4, and 10.0. Release of PAM–Cl at pH 7.4 and at various time intervals from polysiloxane matrices have been given in Table II.

%PAM–Cl Release at pH 7.4

The amount of %PAM–Cl released versus time were plotted for various polysiloxane matrices (Fig. 1). Release of PAM–Cl was very high in the first hour (> 35%), indicating a burst effect in all polysiloxane—PAM–Cl systems. It was slightly lower in the case of P(DM-VM)S (27%). The burst effect observed in these systems may be due to the storage effect (delay between the sample preparation and its release rate measurement), as reported in the literature.[4] Release of PAM–Cl decreases further with an increase of time. The time taken for 80% release of PAM–Cl from various siloxane matrices is given in Table III. PDMS release 80% of the drug in 14 h, whereas other polysiloxane matrices release 80% of PAM–Cl in 5–10 h. After 80% release of PAM–Cl, the release of the drug becomes extremely slow and could not be followed. Total drug release was over in approximately 30–40 h. There was no erosion of matrix during the release rate measurements in phosphate buffer of pH 7.4 at 37°C, retaining the

Table III Time for 80% Release of 2-PAM–Cl from Polysiloxane Matrices at PH 7.4 and 37°C

Sr. No.	Polymer	Time Taken for 80% Release (h)
1	PDMS	14
2	PVMS	7
3	P(DM-VM)S[a]	10
4	P(DM-DE)S[a]	6
5	P(VM-DE)S[a]	5

[a] Copolymer composition = 75 : 25.

Table IV *In Vitro* Release Kinetics of 2-PAM–Cl from Polysiloxane Matrices at PH 3.0 and 37°C

Time (h)	% Release of 2-PAM–Cl from Polysiloxane Matrices				
	PDMS	PVMS	P(DM-VM)S 75 : 25	P(DM-DE)S 75 : 25	P(VM-DE)S 75 : 25
1	34	36	27	38	39
2	43	52	39	54	58
3	49	62	47	63	69
4	56	68	54	73	80
5	60	72	60	80	—
6	64	76	66	—	—
7	68	80	74	—	—
8	71	—	80	—	—
9	73	—	—	—	—
10	76	—	—	—	—
11	78	—	—	—	—
12	80	—	—	—	—

shape and physical integrity for more than 4 weeks. Thus, it appears that drug release occurs purely by a diffusional process. Further, the time taken for 80% release of PAM–Cl using various siloxane matrices was compared, and time changes for different polysiloxane systems were compared (Table III). P(DM-VM)S matrix release 80% drug in 10 h in a acceptable range for slow release formulation. PDMS, being a hydrophobic, nonpolar, and crosslinked polymer, is not releasing the polar PAM–Cl drug and is taking 14 h for releasing 80% of the drug. However, by introduction of vinyl(methyl siloxane) and diethylsiloxane chains in the PDMS matrix, some loosening effect (decrease in packing density) and an increase of flexibility was there, as reported earlier. That is why P(DM-VM)S releases 80% of PAM–Cl in a relatively shorter time (10 h) as compared with PDMS (14 h). Introduction of an ethyl group in the PDMS matrix increases the flexibility of the system and further increases the release rate of PAM–Cl and reduced time for 80% PAM–Cl release (5–6 h), as given in Table III.

Release rates of 2-PAM–Cl from 2-PAM–Cl-loaded polysiloxanes matrices at acidic, (pH 3.0) and basic (pH 10.0) pHs have also been measured in the present studies to examine the influence of pH of the medium on release rate kinetics of 2-PAM–Cl from polysiloxanes matrices.

%PAM–Cl Released at pH 3.0

Amount of PAM–Cl released from polysiloxane systems at pH 3.0 at different time intervals have been measured and are given in Table IV. As shown in Figure 2, the burst effect was observed in all polysiloxane—PAM–Cl systems. This may be due to the storage effect of the polymer–drug systems, as explained earlier.

Also, the time taken for 80% release of PAM–Cl from polysiloxane matrices at pH 3.0 were measured and are given in Table V. PDMS releases

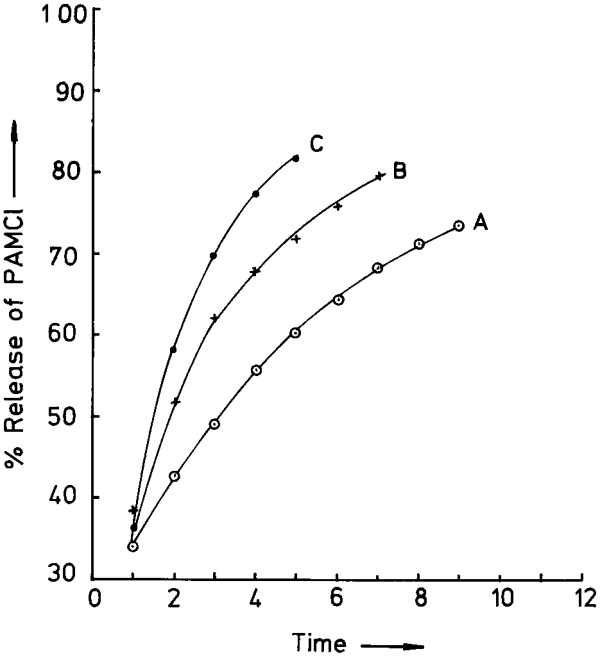


Figure 2 Plot of the percentage of PAM–Cl released versus time for (A) PDMS, (B) PVMS, and (C) P(DM-DE)S at pH 3.0.

Table V Time for 80% Release of 2-PAM–Cl from Polysiloxane Matrices at PH 3.0 and 37°C

Sr. No.	Polymer	Time Taken for 80% Release (h)
1	PDMS	12
2	PVMS	7
3	P(DM-VM)S[a]	8
4	P(DM-DE)S[a]	5
5	P(VM-DE)S[a]	4

[a] Copolymer composition = 75 : 25.

80% of the drug in 12 h, whereas other polysiloxane matrices release 80% of PAM–Cl in 4–8 h at pH 3.0. After 80% of PAM–Cl release, the release of PAM–Cl becomes extremely slow and could not be followed. Further, the times taken for 80% release of PAM–Cl from polysiloxane matrices at pH 3.0 were compared. PVMS releases 80% of PAM–Cl in 7 h, and P(DM-VM)S has taken 8 h to release 80% PAM–Cl. This may be due to the introduction of vinyl group in PDMS that might have increased the flexibility of the system, as explained earlier. Introduction of ethyl groups in PDMS and PVMS further increases the flexibility of the system and increases the release rate of PAM–Cl from P(DM-DE)S and P(VM-DE)S systems. That is why P(DM-DE)S and P(VM-DE)S release PAM–Cl in a relatively shorter time (4–5 h).

Results in Tables II and V show that if the pH of the medium was changed from pH 3.0 to pH 7.4, the time for 80% release changed from 12 to 14 h. Similarly, the time taken for 80% release of PAM–Cl from other polysiloxane matrices were increased to 5–8 h at pH 7.4 in comparison to the release time of 4–7 h at an acidic pH. PVMS releases 80% of the drug in 8 h, whereas P(DM-VM)S releases 80% of the drug in 10 h at pH 7.4, compared to 7 and 8 h at pH 3.0 for PVMS and P(DM-VM)S, respectively. P(DM-DE)S and P(VM-DE)S follow the similar trend of release rate kinetics. P(DM-DE)S releases 80% of PAM–Cl in 6 h, whereas P(VM-DE)S releases 80% of PAM–Cl in 5 h at pH 7.4 compared to 5 and 4 h, respectively, at pH 3.0. Therefore, in all polysiloxane—PAM–Cl systems, a change in pH from 3.0 to 7.4 slowed down the amount of PAM–Cl released from polysiloxane matrices.

%PAM–Cl Release at pH 10.0

Similarly, release rate kinetics of PAM–Cl from polysiloxane matrices at pH 10.0 has also been studied and are given in Table VI. The change of

Table VI *In Vitro* Release Kinetics of PAM–Cl from Polysiloxane Matrices at PH 10.0 and 37°C

	% Release of 2-PAM–Cl from Polysiloxane Matrices				
Time (h)	PDMS	PVMS	P(DM-VM)S (75 : 25)	P(DM-DE)S (75 : 25)	P(VM-DE)S (75 : 25)
1	34	33	27	38	39
2	39	37	33	47	51
3	45	40	40	56	58
4	51	44	54	64	64
5	53	50	58	68	72
6	56	56	62	74	76
7	58	64	65	78	82
8	60	70	69	82	—
9	64	74	71	—	—
10	66	79	74	—	—
11	68	—	77	—	—
12	70	—	80	—	—
13	72	—	—	—	—
14	75	—	—	—	—
15	77	—	—	—	—
16	80	—	—	—	—

Table VII Time for 80% Release of 2-PAM–Cl from Polysiloxane Matrices at PH 10.0 and 37°C

Sr. No.	Polymer	Time Taken for 80% Release (h)
1	PDMS	16 h
2	PVMS	10 h
3	P(DM-VM)S[a]	12 h
4	P(DM-DE)S[a]	7 h, 30 min
5	P(VM-DE)S[a]	6 h, 30 min

[a] Copolymer composition = 75 : 25.

pH to a basic range further slowed down the release rate of PAM–Cl from polysiloxane matrix materials, as indicated by the time taken for 80% release of PAM–Cl from polysiloxane matrices at pH 10.0 (Table VII).

This time taken for 80% release of PAM–Cl increased to 6.5–16 h at a basic pH (pH 10.0). It has been observed that in all polysiloxane—PAM–Cl systems, a change in the pH of the medium from acidic to basic makes the system release PAM–Cl slowly from polysiloxane matrices. This delayed release of PAM–Cl from polysiloxane matrices due to the variation of the pH of the medium from an acidic to a basic pH may be explained on the basis of the dissociation of PAM–Cl and its diffusion through polysiloxane matrices. At an acidic pH, PAM–Cl dissociates to PAM^+Cl^-. Due to dissociation of PAM–Cl at an acidic pH 3.0, the size of the diffusant reduces and increases the rate of release of the drug, and the corresponding time for 80% release of PAM–Cl was less (4–12 h); whereas at the physiological pH (7.4), the dissociation of PAM–Cl is minimum, thereby decreasing the rate of release of PAM–Cl. At a basic pH 10.0, PAM–Cl does not dissociate to PAM^+Cl^-. Therefore, the size of the diffusant is bigger at pH 10.0 in comparison to the size at pH 3.0 and 7.4. Due to the absence of dissociation of PAM–Cl and a bigger size, PAM–Cl takes more time in diffusing out from polysiloxane matrices at pH 10.0.

Thus, the release rate of 2–PAM–Cl(R) from polysiloxane matrices at various pH is found to be in the following order: release rate (R) at pH 3.0 $> R$ at pH 7.4 $> R$ at pH 10.0.

Also, the time for 80% of PAM–Cl release (T) from polysiloxane matrices is in the following order: time for 80% of PAM–Cl release (T) at pH 10.0 $> T$ at pH 7.4 $> T$ at pH 3.0.

Further, the relative amount of PAM–Cl released from polysiloxanes was plotted against $(\text{time})^{1/2}$. This plot results in a straight line, indicating that the order of release of PAM–Cl from polysiloxane matrices follows $\sqrt{t}$ behavior.

Release of PAM–Cl from siloxane matrices is purely based on diffusion process and fits well with the following generalized equation[15]:

$$\frac{M_t}{M_\infty} = Kt^n$$

where M_t is the amount of drug released at time t, M_∞ is the amount of drug released after reaching equilibrium, K is the constant for the characteristic of the polymer–solute (drug) system, and n is the diffusional characteristic of the release mechanism.

From this equation, values of K and n were calculated by plotting log M_t/M_∞ versus log t. Values of n and K are given in Table VIII. The value of n was found to be in the range of 0.26–0.50 for various polysiloxane systems. The value of $n < 0.5$, indicating that the release of PAM–Cl from polysiloxane matrices, follows the Fickian diffusion-controlled mechanism. Diffusion coefficients are calculated using the following equation[15]:

Table VIII Transport Parameter of Polysiloxane—PAM–Cl Systems at Various PHs of the Medium

Polymer	pH	K	n	D
PDMS	3.0	0.35	0.34	3.1×10^{-10}
	7.4	0.34	0.32	5.8×10^{-11}
	10.0	0.34	0.31	5.0×10^{-11}
PVMS	3.0	0.36	0.31	1.4×10^{-9}
	7.4	0.37	0.27	8.9×10^{-10}
	10.0	0.33	0.26	6.4×10^{-10}
P(DM-VM)S[a]	3.0	0.27	0.5	9.1×10^{-10}
	7.4	0.33	0.35	4.9×10^{-10}
	10.0	0.34	0.34	4.0×10^{-10}
P(DM-DE)S[a]	3.0	0.41	0.42	6.7×10^{-9}
	7.4	0.40	0.39	1.1×10^{-9}
	10.0	0.39	0.36	3.9×10^{-10}
P(VM-DE)S[a]	3.0	0.43	0.44	8.1×10^{-8}
	7.4	0.39	0.38	5.7×10^{-9}
	10.0	0.39	0.37	3.1×10^{-9}

[a] Copolymer composition = 75 : 25.

$$\frac{M_t}{M_\infty} = 4(D \cdot t/\pi l^2)^{1/2}$$

where D is the diffusion coefficient of PAM–Cl through polysiloxane matrices, t represents time, and l represents the thickness of the slab.

Diffusion coefficient values for various PAM–Cl-loaded polysiloxane matrix systems have been calculated from the slope of Mt/M versus $t^{1/2}$ and are given in Table VIII. Value of D for the PDMS system is 5.8×10^{-11} cm^2/s at pH 7.4. This value changes to 4.9×10^{-10} cm^2/s in the case of P(DM-VM)S. This indicates that introduction of vinyl methyl siloxane units in PDMS increases the flexibility of P(DM-VM)S system, and, therefore, the D value increases along with the release rate. Also, the value of D is 8.9×10^{10} cm^2/s in the case of PVMS. However, higher values of D at 5.7×10^{-9} and 1.1×10^{-9} cm^2/s for P(VM-DE)S and P(DM-DE)S systems may be due to an increase in the flexibility of these systems. Further, the diffusional characteristic parameter n was found to decrease in each polysiloxane—PAM–Cl system with a change in the pH of the medium from acidic to basic.

The value of D for PDMS at pH 3.0 is 3.14×10^{-10} cm^2/s (Table VIII). This value changes gradually with pH. This value changes to $5.0–10^{-11}$ cm^2/s at pH 10.0. Also, the value of D is 9.1×10^{-10} cm^2/s in the case of P(DM-VM)S at pH 3.0. As the pH was increased from 3.0 to 10.0, the D value found to decrease to 4.0×10^{-10} cm^2/s (Table VIII). In other polysiloxane—PAM–Cl systems that is, the PVMS–PAM–Cl system, the P(DM-DE)S–PAM–Cl system, and the P(VM-DE)S–PAM–Cl system, the same trend of a change in D with a change in pH was observed (Table VIII). Therefore, in all polysiloxane—PAM–Cl systems, as the pH is changed from an acidic to a basic one, the diffusion coefficient D values were found to decrease. This may be due to the dissociation of PAM–Cl at an acidic pH to PAM^+Cl^-. The reduction in size of the diffusant at acidic pH might have caused a change in diffusion coefficient values.

CONCLUSIONS

1. Polysiloxanes having different functional groups (where R equals methyl, ethyl, or vinyl) and respective copolymers have been synthesized by hydrolytic polycondensation of dichlorodialkylsilanes or their mixtures. Polysiloxanes were characterized by viscosity, IR, and NMR techniques.
2. *In vitro* release rate (R) of PAM–Cl from polysiloxanes matrices at various pH is found to be in the following order: release rate (R) at pH 3.0 > R at pH 7.4 > R at pH 10.0.
3. The time for 80% of PAM–Cl release from polysiloxane matrices is in the following order: T at pH 10.0 > T at pH 7.4 > T at pH 3.0.
4. Diffusion coefficient values (D) were found to decrease when the pH is changed from an acidic to a basic one, or D for a particular polysiloxane system is in following the order: D at pH 3.0 > D at pH 7.4 > D at pH 10.0.

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