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Poly(dimethylsiloxane) coatings for controlled drug release—polymer modifications

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Abstract

Modifications of endhydroxylated poly(dimethylsiloxane) (PDMS) formulations were studied for their ability to be applied onto tablet cores in a spray-coating process and to control drug release in zero-order fashion. Modifications of the crosslinker from the most commonly used tetraethylorthosilicate (TEOS) to the trifunctional 3-(2,3-epoxypropoxy)propyltrimethoxysilane (SIG) and a 1:1 mixture of the two were undertaken. Addition of methylpolysiloxane-copolymers were studied. Lactose, microcrystalline cellulose (MCC) and polyethylene glycol 8000 (PEG) were the channeling agents applied. The effects on dispersion properties were characterized by particle size distribution and viscosity. Mechanical properties of resulting free films were studied to determine applicability in a pan-coating process. Release of hydrochlorothiazide (marker drug) was studied from tablets coated in a lab-size conventional coating pan. All dispersions were found suitable for a spray-coating process. Preparation of free films showed that copolymer addition was not possible due to great decline in mechanical properties. Tablets coated with formulations containing PEG were most suitable to control drug release, at only 5% coating weight. Constant release rates could be achieved for formulations with up to 25% PEG; higher amounts resulted in a non-linear release pattern. Upon adding 50% PEG, a drug release of 63% over 24 h could be achieved.

Keywords: Poly(dimethylsiloxane); Controlled drug release; Silicone; Crosslinking; Polyethylene glycol; Elastomer

1. Introduction

Silicone elastomers have been used in the medicinal field for many years and were introduced as potential pharmaceutical tablet coatings in 1988 (Tan et al., 1988) showing a potential for zero-order drug release control. In comparison with commercially existing pharmaceutical tablet coatings, PDMS-elastomers possess several advantages. They do not require plasticizer addition since their glass transition temperatures are below room temperature. They are synthetic substances from a controlled manufacturing process, reducing variability of the product. The resulting latex dispersions are of very low viscosity, even at high solid contents, allowing for economical spray application.

First studies on aqueous based poly(dimethylsiloxane) (PDMS) coatings for the control of drug release from solid oral dosage forms were performed by Li and Peck (1989a) as well as Dahl and Sue (1990). A specific formulation of crosslinked, end-hydroxylated poly(dimethylsiloxane) with the addition of colloidal silica and different molecular weight polyethylene

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glycols (PEG) as channeling agents was successfully used to control drug release from pharmaceutical solid oral dosage forms. The formulation was patented by the company providing the silicone elastomer (Woodard et al., 1994a,b, 1995). Drug release was controlled by the amount and molecular weight of channeling agent added. For up to 12 h, zero-order drug release could be achieved for drugs with varying solubility characteristics (Li and Peck, 1989b; Dahl and Sue, 1992). However, in an evaluation of the coating equipment used, it appeared critical to achieve reproducible release behavior from tablets coated in an air suspension column (Li and Peck, 1990). A less continuous and more permeable coating resulted compared with the pan-coated tablets. Using the latter, potassium chloride release was reduced to 20% within 12 h.

Dahl and Sue (1990) used a pan-coating system to evaluate the effect of curing on tablets coated with the same silicone elastomer as patented by Woodard et al. (1994a). At 19% tablet weight increase, drug release control was achieved. It was determined that after curing for 24 h at 40 °C, 96 h at 60 °C, or 1 h at 80 °C release was similar but significantly lower than for uncured tablets. Curing tablets longer than 1 h at 80 °C resulted in cracking of the coat. Using a formulation containing 35% (of total solids) channeling agent, a maximum of 20% acetaminophen release could be achieved within 24 h, in a zero-order fashion.

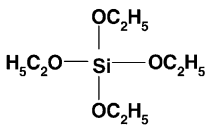
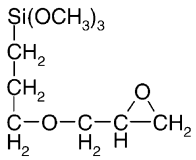
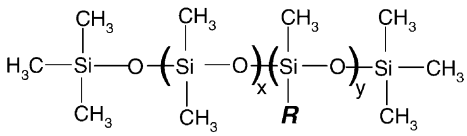
The aim of the presented research was to prepare a formulation of PDMS applicable to be used in a spray-coating process and thereafter to study the effect of modifications of the polymeric network on the dispersion characteristics, on the resulting mechanical strength of the free films, and on drug release from tablets.

2. Materials and methods

2.1. Materials

The following materials were used as received, except for hydrochloric acid that was diluted to 0.1N or 1N solutions as needed. The silicone materials are listed in Table 1. Endhydroxylated poly(dimethylsiloxane) (Q1-3563) of molecular weight 3000 and the

Table 1
Silicone materials, functionality and structures

Material (code)	Function	Structure
Endhydroxylated poly(dimethylsiloxane), molecular weight 3000 (PDMS)	Film former	$HO[(CH_3)_2SiO]_nH$
Tetraethyl orthosilicate (TEOS)	Crosslinker	
3-(2,3-Epoxypropoxy)propyltrimethoxysilane (SIG)	Crosslinker	
Methylpolysiloxane		
R = Dimethyl,methyl (polyethylene oxide) (DC 5324)	Copolymer	$–(CH_2)_3O(CH_2CH_2O)_zH$
R = Poly(oxyethyleneoxy propylene) (DC Q2-5220)	Copolymer	$–C_3H_5O(C_2H_4O)_m(CH_3C_2H_3O)_nH$
R = Polyoxyethylene (DC 193)	Copolymer	$(CH_2)_3O(CH_2CH_2O)_z^-$

methylpolysiloxane copolymeric substances (DC Q2-5220, DC 5324, and DC 193, Dow Corning Corp., Midland, MI, USA), tetraethylorthosilicate and polyethylene glycol of molecular weight 8000 (Aldrich, St. Louis, MO, USA), 3-(2,3-epoxypropoxy)propyltrimethoxysilane (SIG-5840, Gelest Inc., Tullytown, PA, USA), sodium lauryl sulfate, hydrochloric acid 12.1N, sodium phosphate tribasic, certified ACS and Parafilm "M" (Fisher Scientific, Hanover Park, IL, USA), colloidal silica (Aerosil 200, Palmer Suppliers Co., Cleveland, OH, USA), anhydrous lactose (Lactose anhydrous DT, Sheffield-Quest Int., Norwich, NY, USA), microcrystalline cellulose (Emcocel 15M and Emcocel 90M, Penwest Company, Patterson, NY, USA), hydrochlorothiazide (Changzhou Benchi Pharmaceutical Co. Ltd., Changzhou, China) and magnesium stearate (NF-grade, Mallinckrodt Specialty Chemicals Co., St. Louis, MO, USA).

2.2. Methods

2.2.1. Dispersion manufacture

Emulsions of 30% (w/w) PDMS in water were prepared by ultrasonic processing (Vibra Cell High Intensity Ultrasonic Processor Model VC 600, Sonics Materials Inc., Danburry, CT, USA) for 20 min at room temperature with 1% sodium lauryl sulfate as surfactant. Crosslinking of the PDMS was necessary in order to achieve good film formation. The required cross-linking was carried out by mixing the desired amount (1.0–3.5%, w/w) of crosslinking agent (TEOS, SIG or a 1:1 mixture of both) into the PDMS-emulsion, stirring for 10 min at room temperature and adjusting to pH 2 using 1N HCl. The mixtures were then stirred again at room temperature for 10 h. Addition of copolymeric substances or channeling agents was performed after crosslinking through 2 h of intensive magnetic stirring.

2.2.2. Dispersion analysis

Resulting coating dispersions containing 30% (w/w) PDMS were analyzed in duplicate and characterized by particle size distribution (Coulter LS 320, Beckman Coulter Ind., Fullerton, CA, USA) and viscosity (Brookfield viscometer LV-DV II+ with S40 cone, calibrated by silicone viscosity standard (49.2 mPas), sample size 0.5 ml determined at 25 °C; Brookfield, Middleboro, MA, USA).

2.2.3. Free film preparation

Cast films were prepared by pouring 5 g of 30% (w/w) PDMS containing dispersion (without colloidal silica) into an aluminum mold of 4.5 cm diameter and curing at 60 °C until film formation occurred. Sprayed films of diluted coating dispersions (23%, w/w, solids with colloidal silica) were prepared using an air gravity spray gun (Model 43428, Central Pneumatic Professional, Harbor Freight Tools, Camarillo, CA, USA) with a 0.8 mm nozzle on $5 \times 10\,cm^2$ Parafilm® substrate and dried at 50°C with a heat gun (Model 2000D Milwaukee, MHT Products Inc., Plymouth, MN, USA). These films were cured in an oven for 24 h at 50 °C. Samples were stored in a desiccator until analyzed.

2.2.4. Free film analysis

Specimens of approximately $3.0 \times 0.5 \times 0.1\,cm^3$ were cut from each film to analyze the mechanical properties as characterized by Young's modulus. Sample thickness was measured using a digital caliper (Fisherbrand Traceable Digital Caliper, Fisher Scientific). Wen and Mark introduced the instrument used for determination of the equilibrium stress–strain profiles in 1994. Compared to the Instron(r) apparatus applying constantly increasing strain, it was designed to allow step-wise force application, allowing the elastomer to relax prior to determination of the resulting elongation (Wen and Mark, 1994). The instrument was calibrated with 200 and 500 g or 1 kg weights, depending on the strength of the sample. Results were recorded as a mean of three measurements.

2.2.5. Tablet core manufacture

Hydrochlorothiazide was used as a marker drug (solubility 0.70 mg/ml in aqueous media between pH 1 and pH 8; Avdeef et al., 2000). Uncoated tablets were prepared by direct compression in a rotary press (Manesty D3B, Manesty Machines Ltd., Liverpool, England) from a geometric mix of the ingredients, using 9 mm standard concave punches. The average target weight was 250 mg (Table 2).

2.2.6. Tablet core analysis

Tablet cores were analyzed for their physical properties. Analyses were performed on 10 tablets per test. Friability testing was performed for 20 min at 25 rpm (Friabilator, Vankel Industries Inc., Cary, NC, USA)

Table 2
Composition of uncoated tablet cores

Ingredient	Milligram per tablet
Hydrochlorothiazide	10.00
Lactose	118.75
Microcrystalline cellulose	118.75
Silicone dioxide	1.25
Magnesium stearate	1.25
Total	250.00

to avoid any potential capping during tumbling in the coating pan. These tests were performed for 4 × 20 tablets. USP-content uniformity of the tablets was determined prior to coating. Drug release of six tablets each in 0.1N HCl, pH 1.2 and buffer pH 6.8 was tested using USP XXVI-dissolution apparatus 2 (paddles) at 50 rpm until 100% of drug was released.

2.2.7. Tablet coating

The dispersions manufactured containing 30% (w/w) of PDMS (Table 3) were diluted to 23% (w/w) solid content with deionized water. Colloidal silica (10%/25%, w/w of PDMS) was added, if necessary, to increase the mechanical properties of the resulting films. Dispersions were stirred at high-speed for 30 min using a magnetic stirrer to homogenize the samples.

A conventional coating pan (i.d. 15 cm) perforated on the bottom of the pan was used. The coating equipment was specifically designed for this research to allow batch sizes of only 50 g tablets (∼200 tablets). Administration of the coating dispersion was performed using a hand-held, air gravity spray gun with 0.8 mm spray nozzle. Concurrent drying was achieved through application of heated air from a heat gun at 50 °C as used to dry the sprayed films. Coating parameters are described in Table 4. All tablets were cured on trays in an oven for 24 h at 50 °C directly following the coating procedure.

Table 3
Dispersion formulation

Substance	Percent (w/w)
Poly(dimethylsiloxane)	30.0
Crosslinking agent[a]	1.0–3.5
Sodium lauryl sulfate	1.0
Channeling agent or copolymer[b]	0.0/5.0/10.0
Water, deionized	ad 100.0

[a] Used either TEOS, SIG or 1:1 SIG:TEOS.
[b] Percent (w/w) of poly(dimethylsiloxane).

Table 4
Coating parameters

Coating parameter	Value
Batch size (g)	50
Solid content, coating formulation (%)	23
Tablet bed temperature (°C)	50
Atomizing air pressure (psi)	35
Pan speed (rpm)	20
Preheating of cores (min)	5
Spray rate (2 s every 15 s) (g/min)	0.33

2.2.8. Analysis of coated tablets

Drug release was determined over 24 h using USP XXVI-dissolution apparatus 2 (paddles) at 50 rpm for 24 h in 0.1N HCl (pH 1.2), phosphate buffer (pH 6.8) or 2 h in 0.1N HCl (pH 1.2) followed by 22 h in phosphate buffer (pH 6.8). The analyses were performed on six tablets per batch. Drug release rates were determined using linear regression. Similarity of profiles was determined using the f_2-similarity factor based on five different dissolution time points.

3. Results and discussion

3.1. Effects of crosslinking agent

The original coating formulation contained endhydroxylated poly(dimethylsiloxane) crosslinked with the most commonly used, tetrafunctional crosslinking agent tetraethylorthosilicate (TEOS). Changing the crosslinking agent from TEOS to the trifunctional 3-(2,3-epoxypropoxy)propyltrimethoxysilane (SIG) with the 2,3-epoxypropoxy functional group resulted in coating emulsions with particle size distribution similar to the one achieved from PDMS crosslinked with 1% (w/w) TEOS (Fig. 1). The particle size distribution was unimodal and all particles were below 1 μm in diameter.

The viscosity of the modified emulsions was between 4 and 6 mPas. Addition of colloidal silica increased the viscosity of the dispersion. The effect was negligible (2 mPas) when going from zero to 10% (w/w of PDMS) of silica. Addition of 25% (w/w of

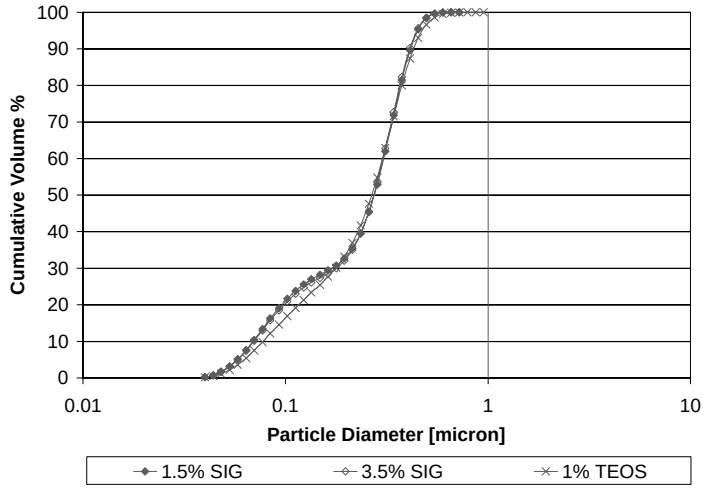


Fig. 1. Particle size distribution of coating dispersions (30% PDMS) with different type and amount of crosslinking agents.

PDMS) silica resulted in a 10 mPas increase in viscosity (data not presented). Nevertheless, for the spray gun used, a viscosity up to 60 mPas would be acceptable (Central Pneumatic, operating instructions).

Cast films from 1% (w/w) TEOS-crosslinked networks were significantly stronger (P-value <0.05) than 1.5% (w/w) SIG-crosslinked networks or, in other words, the SIG-crosslinked PDMS at stoichiometrically corresponding concentrations of crosslinking agent was more elastomeric (Table 5). As one SIG-molecule would only react with three PDMS-chains, a more flexible and less dense network structure was created. Additionally, higher amounts of crosslinking agent resulted in increased mechanical properties of the free films. Even though 1.0% (w/w) TEOS would represent a stoichiometric amount of crosslinker, it was likely that not all hydrolyzed crosslinker had been transported into the oil phase. Thus, at higher concentrations of TEOS or SIG, more hydrolyzed crosslinking agent passed into the PDMS-phase, allowing for more crosslinking to occur and a denser, stronger network was created.

Table 5
Effect of crosslinking agent on mechanical properties of the free films, cast and sprayed

Sample characteristics		Modulus (MPa) (S.D.)
Cast films		
TEOS	1%	0.129 (0.003)
SIG	1.5%	0.064 (0.001)
	3.5%	0.166 (0.005)
Sprayed films with 10% colloidal silica		
TEOS	1%	0.281 (0.014)
SIG	1.5%	0.108 (0.011)
	3.5%	0.629 (0.017)

TEOS-networks were also stronger through in situ created SiO_2 particles, with greater effects at higher TEOS-concentrations, as has been reported in literature previously (Sur and Mark, 1988).

Application onto tablet cores was first performed using formulations containing 25% (w/w of PDMS) colloidal silica. Dissolution studies showed that no drug would be released from tablets coated at a 10% coating weight for any of the three different formulations. For tablets coated with the new SIG-crosslinking agent even coating weights of 5% were sufficient to protect the tablet core. Below these limits, film coats would break within the first hour of dissolution prior to any drug release.

The reduced lower limit of coating weight for the SIG-crosslinked films was probably the result of the greater elastomeric properties of these films. Upon penetration of water into the tablet core the osmotic pressure would rise and result in breakage of the coat. SIG-crosslinked films, however, were able to initially deform and only, when the limit for deformation would be reached, tablet coat breakage occurred.

Thus, a 3.5% (w/w) SIG-crosslinked polymer was preferred for further studies. SIG had the advantage

over TEOS of introducing an epoxy functional group without a negative effect on the tablet film surface properties. Tablet film coats remained intact even at lower coating weight, thus potentially being a more economical coating material. Additionally, 3.5% SIG-crosslinked films with 10% (w/w of PDMS) silica were stronger (0.629 MPa) than the original TEOS-formulation with 10% colloidal silica (0.281 MPa, P-value <0.05). Therefore, the use of the formulation with 10% (w/w of PDMS) colloidal silica in tablet coating formulations was preferred.

3.2. Effects of copolymeric substances

Tablets with TEOS or SIG-crosslinked PDMS and 10% (w/w of PDMS) colloidal silica addition did not release any drug during 24 h in 0.1N HCl (pH 1.2) or phosphate buffer (pH 6.8) at coating weights of >5%. For coating weights below 5% the film coats were not strong enough to protect the tablet core. Cracks in the film coating were observed upon exposure to the dissolution media resulting in immediate drug release.

All tested copolymer additions resulted in a great reduction of the Young's modulus (Table 6). The effects were most pronounced for DC 193 > DC 5324 > DC Q2-5220. Spray application onto tablet cores was not possible for formulations with copolymers DC 193 or DC 5324. No coherent tablet coat could be achieved, as films were too weak to withstand the stress of the pan-coating process. However, a coating of 3.5% SIG-crosslinked PDMS, 10% (w/w of PDMS) DC Q2-5220 and 10% (w/w of PDMS) colloidal silica could successfully be applied. But during the first 1.5 h of dissolution, tablet coats opened prior to any drug release. Only a formulation of 10% (w/w of PDMS) DC Q2-5220 to 1.5% (w/w) SIG-crosslinked PDMS resulted in a film coat that was more elastomeric and thus able to withstand better the osmotic pressure buildup after penetration of water. The release profile was zero-order, but limited to a maximum of 10% drug release in 24 h. Further increase in the amount of DC Q2-5220 and increased amount of crosslinking agent were not successful in achieving sufficient mechanical properties to allow for drug release control.

3.3. Effects of channeling agents

Addition of only 5% (w/w of PDMS) water-soluble lactose to 3.5% SIG-crosslinked PDMS resulted in a similar zero-order release profile with a maximum of 10% release over 24 h in 0.1N HCl, pH 1.2, and phosphate buffer pH 6.8. However, increasing the amount of channeling agent to 10% did not allow for drug release control. Tablet film coats were too weak resulting in breakage of the coat when exposed to aqueous media prior to any drug release.

Films with 10% (w/w of PDMS) water-insoluble microcrystalline cellulose (15 nm average particle size) to 3.5% SIG-crosslinked PDMS were sufficiently strong to protect the tablet core but did not result in any greater drug release than a maximum of 10% after 24 h in both media (zero-order).

Addition of the water-soluble channeling agent polyethylene glycol (molecular weight 8000) therefore was more promising. An addition of 10% (w/w of PDMS) to the 3.5% SIG-crosslinked PDMS dispersion resulted in a constant release rate with a maximum of 20% drug released after 24 h in 0.1N HCl. The release rate in buffer pH 6.8 was slightly slower and maximum release was reduced by 5% (Fig. 2). However, release profiles were still similar (f_2-similarity factor 71).

Table 6
Effect of copolymer addition to 3.5% SIG-crosslinked PDMS on the mechanical properties of the free, cast film without silica addition

	Materials						
	Contents (w/w of PDMS)						
	Without copolymer	DC 193		DC Q2-5220		DC 5324	
		5%	10%	5%	10%	5%	10%
Modulus (MPa) (S.D.)	0.166 (0.005)	0.057 (0.006)	0.029 (0.002)	0.078 (0.002)	0.056 (0.002)	0.044 (0.004)	0.034 (0.005)

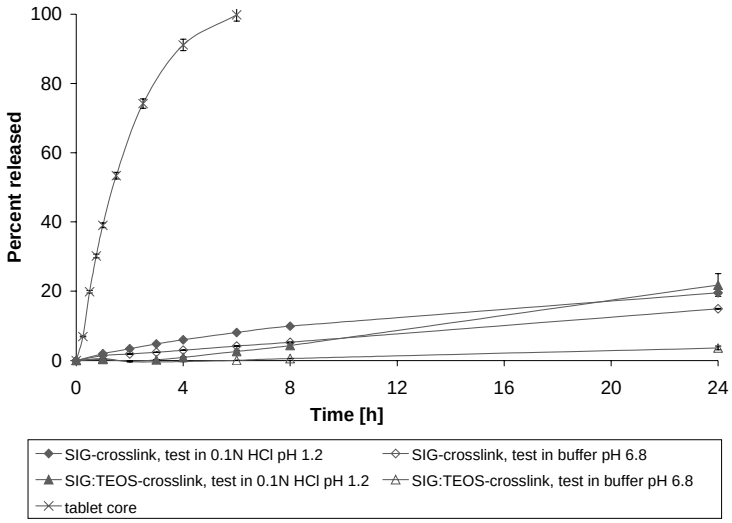


Fig. 2. Hydrochlorothiazide release from tablets coated with 3.5% SIG or SIG:TEOS (1:1)-crosslinked PDMS, containing 10% polyethylene glycol (molecular weight 8000) and 10% colloidal silica, in different media at 5% coating weight.

3.4. Effects of a mixture of crosslinking agents

Changing from the 3.5% SIG-crosslink to a 3.5% SIG:TEOS 1:1 mixture-crosslink resulted in films of greater mechanical strength, as can be seen in the five-fold increased value for the modulus (Table 7). Drug release in 0.1N HCl resulted in the same maximum release of 20% after 24 h (Fig. 2). However, a lag time of 3 h was observed and drug release was very much reduced in buffer pH 6.8. Dissolution of the tablet following immersion for 2 h in 0.1N HCl followed by 22 h in buffer pH 6.8 resulted in a similar release profile (f_2-similarity factor 85) to the one achieved in 0.1N HCl (Fig. 3). Since swelling of the coated tablets was reduced in basic media, release rates were reduced. If, however, tablets were allowed to swell in 0.1N HCl, the release rate in buffer pH 6.8 was similar to the one achieved in 0.1N HCl alone. This was observed for all the samples containing the mixture of crosslinking agents.

As films had increased mechanical strength, coating without addition of colloidal silica was possible. Omitting the silica eliminated an additional diffusion barrier and in result, drug release increased by 10% when tested for 2 h in 0.1N HCl pH 1.2 followed by 22 h in buffer pH 6.8 (Fig. 4). Additionally, the previously noticed lag time did not occur.

Even after increasing the amount of polyethylene glycol, the particle size distribution remained good (Fig. 5). The increase in mean particle size after addition of PEG was not statistically significant (P-value >0.05). As PEG contains hydroxylgroups, an interaction with the surfactant (e.g. through hydrogen bonding around the PDMS-micelles) could result in a larger droplet size. An interaction with the PDMS was excluded. Penetration of a hydrophilic substance into the hydrophobic PDMS was very unlikely and differential scanning calorimetry analyses by Li and Peck (1989a) had previously shown that such interaction would not occur. Compared to the formulation without polyethylene glycol, 90% of the particles were below 1 μm, 10% less than the original formulation. However, no particles were greater than 5 μm. Thus, no negative effect on film formation was expected (Lehman, 1997).

Table 7
Effect of crosslinking agent combination on mechanical properties of the free, cast film without silica addition

	Crosslinking agent (3.5%, w/w)		
	TEOS	SIG	SIG:TEOS (1:1)
Modulus (MPa) (SD)	0.209 (0.005)	0.166 (0.005)	1.07 (0.01)

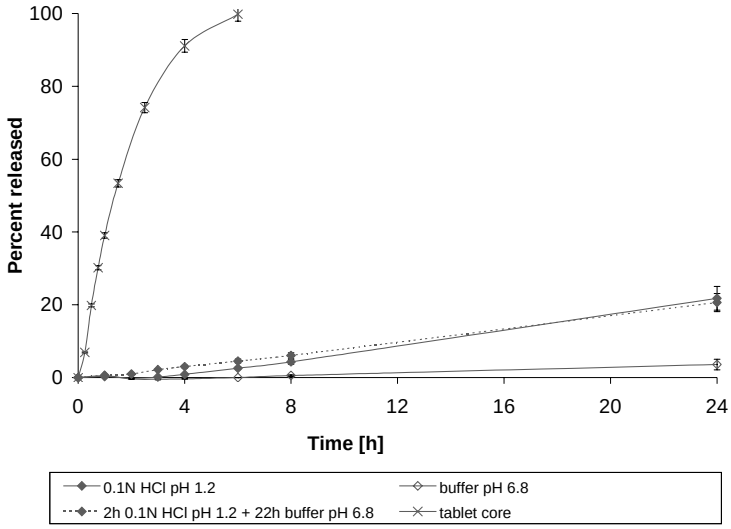


Fig. 3. Hydrochlorothiazide release from tablets coated with 3.5% SIG:TEOS (1:1)-crosslinked PDMS, containing 10% polyethylene glycol (molecular weight 8000) and 10% colloidal silica, in different media at 5% coating weight.

When increasing the amount of polyethylene glycol to 25 and 50% (w/w of PDMS) the Young's modulus significantly increased (P-values <0.05) resulting in still strong but more brittle and less elastomeric films (Table 8). An increase in drug release up to 46 and 62% over 24 h could be achieved (Fig. 6). For the TEOS-crosslinked network Li and Peck (1989c) had previously demonstrated that drug release would occur through pores created in the PDMS-network after

Table 8
Effect of polyethylene glycol on the mechanical properties of sprayed films from 3.5% SIG:TEOS (1:1)-crosslinked PDMS, no colloidal silica

PEG-amount (%)	Young's modulus (MPa) (S.D.)
0	0.409 (0.027)
10	0.788 (0.070)
25	6.79 (0.26)
50	8.46 (0.28)

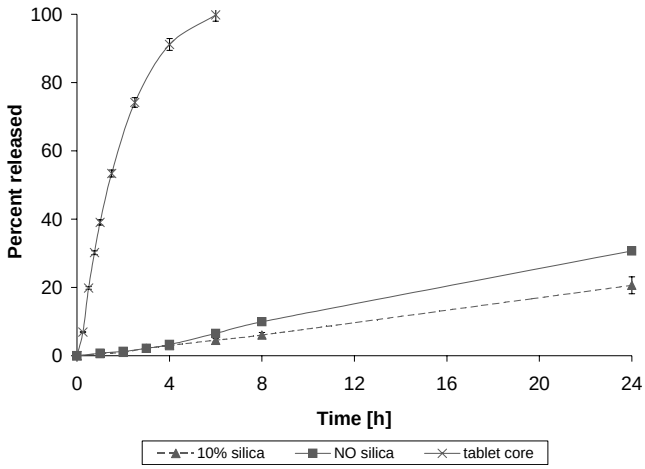


Fig. 4. Hydrochlorothiazide release from tablets coated with 3.5% SIG:TEOS (1:1)-crosslinked PDMS containing 10% polyethylene glycol (molecular weight 8000) at 5% coating weight, with 10% and without colloidal silica; dissolution of 2 h 0.1N HCl followed by 22 h buffer pH 6.8.

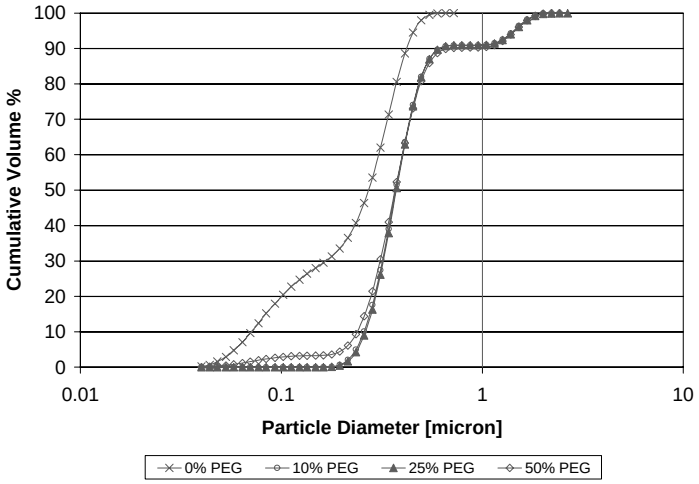


Fig. 5. Particle size distribution of coating dispersions (30% PDMS) with different amount of polyethylene glycol to 3.5% SIG:TEOS 1:1 crosslinked PDMS.

the PEG was dissolved and leached out into the dissolution media. This mechanism of drug release was assumed to be applicable for the newly crosslinked formulation as well. Therefore, drug release increased with increasing amounts of PEG added, as a more porous tablet coat was created. Drug release was linear at 10 and 25% (w/w of PDMS) PEG addition, with release rates of 1.24 and 1.95% per hour. For the formulation containing 50% polyethylene glycol it was noticed, however, that the initial lag time of 2 h was more pronounced and a non-linear release profile resulted.

To test whether reproducible drug release was achieved, a second batch of coating dispersion was prepared and coated onto tablet cores from the same batch under the same coating conditions. The obtained release profiles were similar (f_2-similarity factor 98).

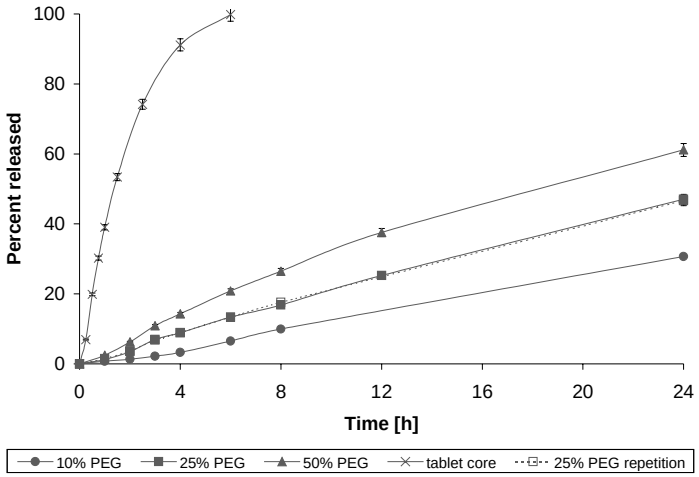


Fig. 6. Hydrochlorothiazide release from tablets coated with 3.5% SIG:TEOS (1:1)-crosslinked PDMS containing 10, 25, or 50% polyethylene glycol (molecular weight 8000) at 5% coating weight without colloidal silica; dissolution media 2 h 0.1N HCl pH 1.2 followed by 22 h buffer pH 6.8; repetition of coating results with a different batch of coating dispersion on tablet cores from the same batch.

4. Conclusions

Formulations of poly(dimethylsiloxane) were manufactured that did not require plasticizer addition and did not show any tackiness when applied onto tablet cores in a spray-coating process. This represents a formulation advantage over almost all other commercially available coating dispersions. The PDMS was crosslinked into a polymeric network that was able to form a strong film without addition of colloidal silica, allowing greater ease during spray application since constant stirring can be avoided and no settlement of solids can occur. Drug release could be controlled by varying the amount of polyethylene glycol (molecular weight 8000) added, whereas addition of other channeling agents, lactose or microcrystalline cellulose, were unsuccessful in achieving sufficient release without losing mechanical strength of the resulting film coat. The same was true for copolymers added to the coating dispersion. A maximum release of 62% over a period of 24 h could be achieved, when adding 50% (w/w of PDMS) polyethylene glycol to a formulation of PDMS crosslinked with a 3.5% mixture of SIG:TEOS (1:1). The release profile was linear only up to an amount of 25% PEG added. At higher amounts of PEG the effect of initial swelling of the polymer was expressed in a reduced initial release. The reproducibility of drug release from a different batch of coating material was demonstrated. The PDMS formulation thus allowed reliable drug release control.

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References

Avdeef, A., Berger, C.M., Brownell, C., 2000. pH-metric solubility. 2: correlation between the acid-base titration and the Saturation shake-flask solubility-pH methods. Pharm. Res. 17, 85–89.

Dahl, T.C., Sue, I.T., 1990. The effects of heat and desiccation treatment on the controlled release properties of aqueous silicone latex coated tablets. Drug Dev. Ind. Pharm. 16, 2097–2107.

Dahl, T.C., Sue, I.T., 1992. Mechanisms to control drug release from pellets coated with a silicone elastomer aqueous dispersion. Pharm. Res. 9, 398–405.

Lehman, K., 1997. Chemistry and application properties of polymethacrylate coating systems. In: McGinity, J.W. (Ed.), Aqueous Polymeric Coatings for Pharmaceutical Dosage Forms, 2nd ed. Marcel Dekker, New York, pp. 101–176.

Li, L.C., Peck, G.E., 1989a. Water based silicone elastomer controlled release tablet film coating 1: free film evaluation. Drug Dev. Ind. Pharm. 15, 65–95.

Li, L.C., Peck, G.E., 1989b. Water based silicone elastomer controlled release tablet film coating II—formulation considerations and coating evaluation. Drug Dev. Ind. Pharm. 15, 499–531.

Li, L.C., Peck, G.E., 1989c. Water based silicone elastomer controlled release tablet film coating III—drug release mechanism. Drug Dev. Ind. Pharm. 15, 1943–1968.

Li, L.C., Peck, G.E., 1990. Water based silicone elastomer controlled release tablet film coating IV: process evaluation. Drug Dev. Ind. Pharm. 16, 415–435.

Sur, G.S., Mark, J.E., 1988. Grafting of polymer onto filler particles used to reinforce an elastomer. Polym. Bull. 20, 131–136.

Tan, E.L., Liu, J.C., Chien, Y.W., 1988. Controlled drug release from silicone coated tablets: preliminary evaluation of coating techniques and characterization of membrane permeation kinetics. Int. J. Pharm. 42, 161–169.

Wen, J., Mark, J.E., 1994. Torsion studies of thermoelasticity and stress–strain isotherms of unimodal, bimodal, and filled networks of poly(dimethylsiloxane). Polym. J. 26, 151–157.

Woodard, J.T., Musolf, M.C., Miller, P.J., 1994a. Process for forming a coated active agent-containing article. U.S. Patent 5,310,572.

Woodard, J.T., Musolf, M.C., Miller, P.J., 1994b. Aqueous film-forming compositions for controlling the release of active agents. U.S. Patent 5,358,990.

Woodard, J.T., Musolf, M.C., Miller, P.J., 1995. Coated active agent-containing article. U.S. Patent 5,401,515.