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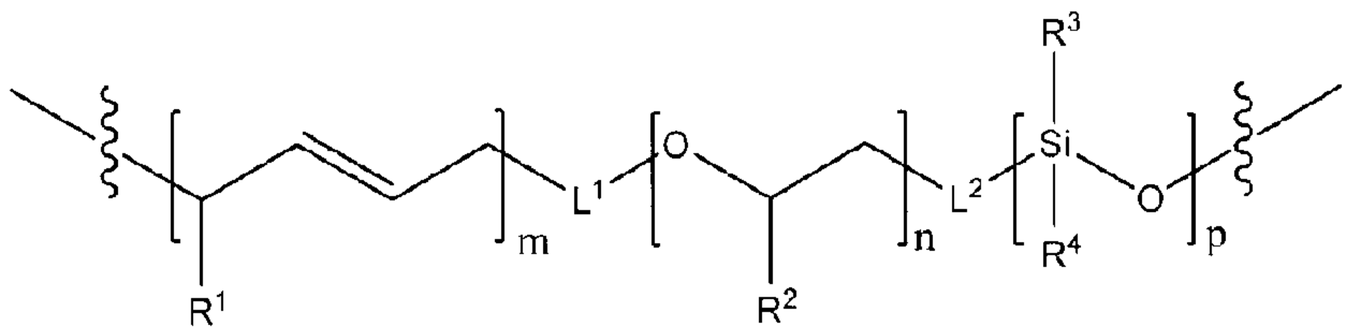
(54) Titre : BIOMATERIAUX RENFERMANT DES COPOLYMERES TRIBLOCS DE POLYBUTADIENE-POLY ALKYLE ETHER POLYSILOXANE

(54) Title: BIOMATERIALS COMPRISING POLYBUTADIENE-POLYALKYLETHERPOLYSILOXANE TRI-BLOCK COPOLYMERS



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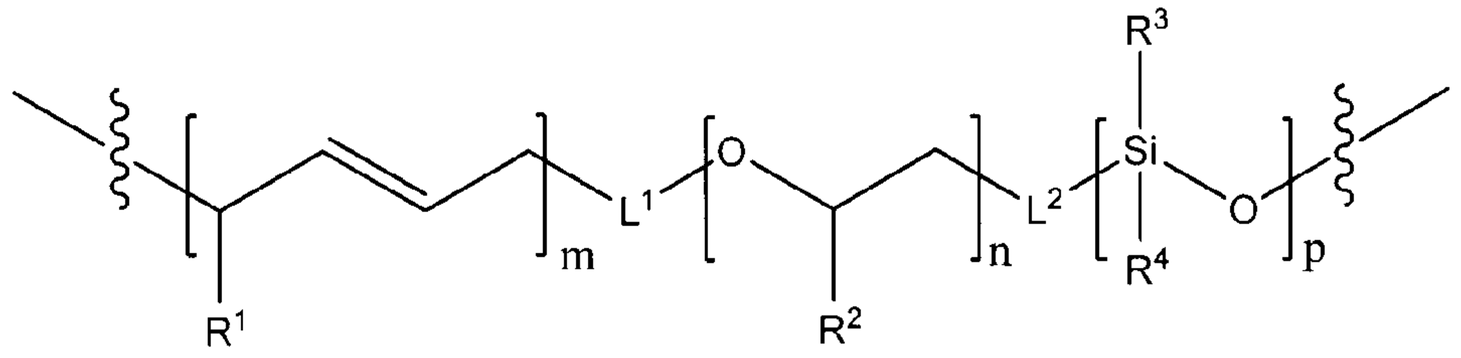
(57) Abrégé/Abstract:
The present invention provides a triblock copolymer of formula I

(see formula I)

and a viscoelastic biostable foam comprising the same.

ABSTRACT

The present invention provides a triblock copolymer of formula I



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and a viscoelastic biostable foam comprising the same.

WO 2011/073967 PCT/IE2010/000073

Biomaterials Comprising Polybutadiene-polyalkyletherpolysiloxane Tri-Block Copolymers

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] The present application claims the benefit of United States provisional patent application number 61/287,909, filed December 18, 2009.

FIELD OF THE INVENTION

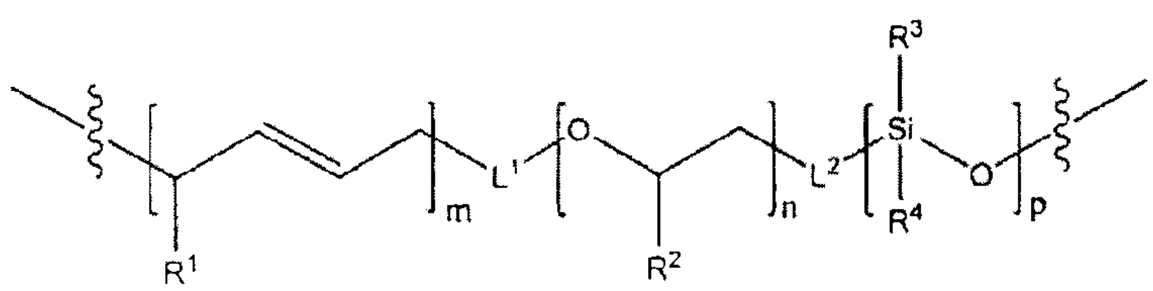
[0002] The invention relates to biomedical materials and in particular to materials that are mechanically and chemically stable in the harsh environment of the digestive system.

BACKGROUND OF THE INVENTION

[0003] It has been found that in addition to the low pH and digestive enzymes of the stomach, that digestive enzymes, which originate in the pancreas are particularly effective at degrading various food constituents. Many medical devices are used in this part of the anatomy for reflux control, biliary drainage catheters, biliary stents and obesity devices. The biomaterials that are currently being used for these applications include siloxanes, polyether polyurethanes and polycarbonate polyurethanes. These materials suffer from a variety of degradation mechanisms attributable to either enzymes in the stomach or intestines or the extremes of high and low pH that exists in the intestines and stomach respectively.

SUMMARY OF THE INVENTION

[0004] According to certain embodiments of the invention there is provided a triblock copolymer of formula [polybutadiene][polyalkyl ether][polysiloxane], *e.g.*, a triblock copolymer of formula **I**:



I

I

wherein the copolymers are chemically interspersed (bound) between urethane and/or urea linkages and wherein each of m, n, p, L^1, L^2, R^1, R^2, R^3, and R^4 is as defined and described herein.

[0005] In certain embodiments, the present invention provides a biomaterial comprising a provided copolymer as defined and described herein. In certain embodiments, the present invention provides a medical device comprising a provide copolymer as defined and described herein.

[0006] In certain embodiments, the present invention provides a polyurethane/urea foam comprising a provided copolymer as defined and described herein. In certain embodiments, the present invention provides a biostable viscoelastic foam comprising a provided copolymer as defined and described herein.

[0007] In some embodiments, the present invention provides a pre-formed soft segment for a polyurethane / urea foam wherein the soft segment is of formula **I** as defined and described herein.

BRIEF DESCRIPTION OF THE DRAWINGS

[0008] **Figure 1** is a graph of valve performance over time in a simulated gastric fluid, where the performance ciriterion is the opening pressure of the valve.

[0009] **Figure 2** is a graph of mass uptake over time for biomaterials of the invention.

[0010] **Figure 3** is a comparison of the chemical stability of a BAS triblock urethane polymer of the invention.

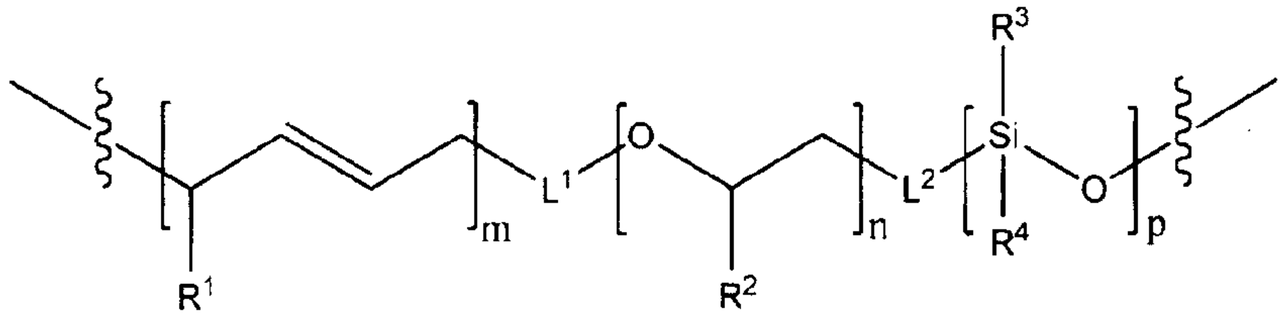
DETAILED DESCRIPTION OF CERTAIN EMBODIMENTS

1. General Description:

[0011] Described herein are urethane/urea triblock copolymers and associated foams made from alternating blocks of butadiene, siloxane, and alkylether polymers, which are chemically and mechanically stable in the environment of the digestive system. The block copolymers may comprise siloxane, alkyl ether and alkylene polymers wherein either all three or two of the blocks are linked via urethane / urea functional groups.

[0012] In some embodiments, the present invention provides a multiblock copolymer that is biomimetic and hydrolytically stable in a gastric environment. Such multiblock copolymers are

triblock copolymers of the formula [polybutadiene][polyalkyl ether][polysiloxane]. In certain embodiments, provided multiblock copolymers are of formula I:



I

wherein:

each ~ represents a point of attachment to a urethane or urea linkage;

each of R^1, R^2, R^3, and R^4 is independently selected from one or more of halogen, R, OR, $-CO_2R$, a fluorinated hydrocarbon, a polyether, a polyester or a fluoropolymer;

each R is independently hydrogen, an optionally substituted C_{1-20} aliphatic group, or an optionally substituted group selected from phenyl, 8-10 membered bicyclic aryl, a 4-8 membered monocyclic saturated or partially unsaturated heterocyclic ring having 1-2 heteroatoms independently selected from nitrogen, oxygen, or sulphur, or 5-6 membered monocyclic or 8-10 membered bicyclic heteroaryl group having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

each of m n and p is independently 2 to 100; and

each of L^1 and L^2 is independently a bivalent C_{1-20} hydrocarbon chain wherein 1-4 methylene units of the hydrocarbon chain are optionally and independently replaced by –O-, -S-, -N(R)C(O)O-, -N(R)C(O)N(R)-, -OC(O)N(R)-, -N(R)-, -C(O)-, -C(O)N(R)-, -N(R)C(O)-, $-SO_2-$, $-SO_2N(R)-$, $-N(R)SO_2-$, -OC(O)-, –C(O)O-, or a bivalent cycloalkylene, arylene, heterocyclene, or heteroarylene.

[0013] In certain embodiments, a provided copolymer comprises alternating blocks of butadiene (B), alkylether (A) and Siloxane (S) that are linked together with urethane/urea linkages.

[0014] In certain embodiments, a provided copolymer is used for a medical device to be used in the digestive system and other anatomical regions that have high concentrations of enzymes and other degrading species.

[0015] In certain embodiments, a provided copolymer has low water uptake thus contributing to improved chemical stability.

[0016] In certain embodiments, provided copolymers are biocompatible. In certain embodiments, a provided copolymer has high elongation, flexibility, chemical and mechanical stability in harsh environments.

[0017] In certain embodiments, a provided copolymer shows improved performance in terms of water uptake as shown in Figure 2 and chemical stability/biodurability as shown in Figure 1 and Figure 3.

2. Definitions:

[0018] Compounds of this invention include those described generally above, and are further illustrated by the classes, subclasses, and species disclosed herein. As used herein, the following definitions shall apply unless otherwise indicated. For purposes of this invention, the chemical elements are identified in accordance with the Periodic Table of the Elements, CAS version, Handbook of Chemistry and Physics, 75th Ed. Additionally, general principles of organic chemistry are described in "Organic Chemistry", Thomas Sorrell, University Science Books, Sausalito: 1999, and "March's Advanced Organic Chemistry", 5th Ed., Ed.: Smith, M.B. and March, J., John Wiley & Sons, New York: 2001,

[0019] As described herein, compounds of the invention may optionally be substituted with one or more substituents, such as are illustrated generally above, or as exemplified by particular classes, subclasses, and species of the invention. It will be appreciated that the phrase "optionally substituted" is used interchangeably with the phrase "substituted or unsubstituted." In general, the term "substituted", whether preceded by the term "optionally" or not, refers to the replacement of hydrogen radicals in a given structure with the radical of a specified substituent. Unless otherwise indicated, an optionally substituted group may have a substituent at each substitutable position of the group, and when more than one position in any given structure may be substituted with more than one substituent selected from a specified group, the substituent may be either the same or different at every position. Combinations of substituents envisioned by this invention are preferably those that result in the formation of stable or chemically feasible compounds. The term "stable", as used herein, refers to compounds that are not substantially

altered when subjected to conditions to allow for their production, detection, and preferably their recovery, purification, and use for one or more of the purposes disclosed herein. In some embodiments, a stable compound or chemically feasible compound is one that is not substantially altered when kept at a temperature of 40°C or less, in the absence of moisture or other chemically reactive conditions, for at least a week.

[0020] The term "aliphatic" or "aliphatic group", as used herein, denotes a hydrocarbon moiety that may be straight-chain (i.e., unbranched), branched, or cyclic (including fused, bridging, and spiro-fused polycyclic) and may be completely saturated or may contain one or more units of unsaturation, but which is not aromatic. Unless otherwise specified, aliphatic groups contain 1–20 carbon atoms. In some embodiments, aliphatic groups contain 1–10 carbon atoms. In other embodiments, aliphatic groups contain 1–8 carbon atoms. In still other embodiments, aliphatic groups contain 1–6 carbon atoms, and in yet other embodiments aliphatic groups contain 1–4 carbon atoms. Suitable aliphatic groups include, but are not limited to, linear or branched, alkyl, alkenyl, and alkynyl groups, and hybrids thereof such as (cycloalkyl)alkyl, (cycloalkenyl)alkyl or (cycloalkyl)alkenyl.

[0021] The term "lower alkyl" refers to a C_{1-4} straight or branched alkyl group. Exemplary lower alkyl groups are methyl, ethyl, propyl, isopropyl, butyl, isobutyl, and tert-butyl.

[0022] The term "lower haloalkyl" refers to a C_{1-4} straight or branched alkyl group that is substituted with one or more halogen atoms.

[0023] The term "heteroatom" means one or more of oxygen, sulfur, nitrogen, phosphorus, or silicon (including, any oxidized form of nitrogen, sulfur, phosphorus, or silicon; the quaternized form of any basic nitrogen or; a substitutable nitrogen of a heterocyclic ring, for example N (as in 3,4-dihydro-2*H*-pyrrolyl), NH (as in pyrrolidinyl) or NR^+ (as in N-substituted pyrrolidinyl)).

[0024] The term "unsaturated", as used herein, means that a moiety has one or more units of unsaturation.

[0025] As used herein, the term "bivalent C_{1-8} [or C_{1-6}] saturated or unsaturated, straight or branched, hydrocarbon chain", refers to bivalent alkylene, alkenylene, and alkynylene chains that are straight or branched as defined herein.

[0026] The term "alkylene" refers to a bivalent alkyl group. An "alkylene chain" is a polymethylene group, i.e., $-(CH_2)_n-$, wherein n is a positive integer, preferably from 1 to 6, from

1 to 4, from 1 to 3, from 1 to 2, or from 2 to 3. A substituted alkylene chain is a polymethylene group in which one or more methylene hydrogen atoms are replaced with a substituent. Suitable substituents include those described below for a substituted aliphatic group.

[0027] The term "alkenylene" refers to a bivalent alkenyl group. A substituted alkenylene chain is a polymethylene group containing at least one double bond in which one or more hydrogen atoms are replaced with a substituent. Suitable substituents include those described below for a substituted aliphatic group.

[0028] The term "halogen" means F, Cl, Br, or I.

[0029] The term "aryl" used alone or as part of a larger moiety as in "aralkyl", "aralkoxy", or "aryloxyalkyl", refers to monocyclic or bicyclic ring systems having a total of five to fourteen ring members, wherein at least one ring in the system is aromatic and wherein each ring in the system contains 3 to 7 ring members. The term "aryl" may be used interchangeably with the term "aryl ring".

[0030] As described herein, compounds of the invention may contain "optionally substituted" moieties. In general, the term "substituted", whether preceded by the term "optionally" or not, means that one or more hydrogens of the designated moiety are replaced with a suitable substituent. Unless otherwise indicated, an "optionally substituted" group may have a suitable substituent at each substitutable position of the group, and when more than one position in any given structure may be substituted with more than one substituent selected from a specified group, the substituent may be either the same or different at every position. Combinations of substituents envisioned by this invention are preferably those that result in the formation of stable or chemically feasible compounds. The term "stable", as used herein, refers to compounds that are not substantially altered when subjected to conditions to allow for their production, detection, and, in certain embodiments, their recovery, purification, and use for one or more of the purposes disclosed herein.

[0031] Suitable monovalent substituents on a substitutable carbon atom of an "optionally substituted" group are independently halogen; $-(CH_2)_{0-4}R^\circ$; $-(CH_2)_{0-4}OR^\circ$; $-O-(CH_2)_{0-4}C(O)OR^\circ$; $-(CH_2)_{0-4}CH(OR^\circ)_2$; $-(CH_2)_{0-4}SR^\circ$; $-(CH_2)_{0-4}Ph$, which may be substituted with R°; $-(CH_2)_{0-4}O(CH_2)_{0-1}Ph$ which may be substituted with R°; $-CH=CHPh$, which may be substituted with R°; $-NO_2$; $-CN$; $-N_3$; $-(CH_2)_{0-4}N(R^\circ)_2$; $-(CH_2)_{0-4}N(R^\circ)C(O)R^\circ$; $-N(R^\circ)C(S)R^\circ$; $-(CH_2)_{0-4}N(R^\circ)C(O)NR^\circ_2$; $-N(R^\circ)C(S)NR^\circ_2$; $-(CH_2)_{0-4}N(R^\circ)C(O)OR^\circ$; $-N(R^\circ)N(R^\circ)C(O)R^\circ$;

-N(R°)N(R°)C(O)NR°$_2$; -N(R°)N(R°)C(O)OR°; -(CH$_2$)$_{0-4}$C(O)R°; -C(S)R°; -(CH$_2$)$_{0-4}$C(O)OR°; -(CH$_2$)$_{0-4}$C(O)SR°; -(CH$_2$)$_{0-4}$C(O)OSiR°$_3$; -(CH$_2$)$_{0-4}$OC(O)R°; -OC(O)(CH$_2$)$_{0-4}$SR-, SC(S)SR°; -(CH$_2$)$_{0-4}$SC(O)R°; -(CH$_2$)$_{0-4}$C(O)NR°$_2$; -C(S)NR°$_2$; -C(S)SR°; -SC(S)SR°, -(CH$_2$)$_{0-4}$OC(O)NR°$_2$; -C(O)N(OR°)R°; -C(O)C(O)R°; -C(O)CH$_2$C(O)R°; -C(NOR°)R°; -(CH$_2$)$_{0-4}$SSR°; -(CH$_2$)$_{0-4}$S(O)$_2$R°; -(CH$_2$)$_{0-4}$S(O)$_2$OR°; -(CH$_2$)$_{0-4}$OS(O)$_2$R°; -S(O)$_2$NR°$_2$; -(CH$_2$)$_{0-4}$S(O)R°; -N(R°)S(O)$_2$NR°$_2$; -N(R°)S(O)$_2$R°; -N(OR°)R°; -C(NH)NR°$_2$; -P(O)$_2$R°; -P(O)R°$_2$; -OP(O)R°$_2$; -OP(O)(OR°)$_2$; SiR°$_3$; -(C$_{1-4}$ straight or branched alkylene)O-N(R°)$_2$; or -(C$_{1-4}$ straight or branched alkylene)C(O)O-N(R°)$_2$, wherein each R° may be substituted as defined below and is independently hydrogen, C$_{1-6}$ aliphatic, -CH$_2$Ph, -O(CH$_2$)$_{0-1}$Ph, or a 5–6-membered saturated, partially unsaturated, or aryl ring having 0–4 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or, notwithstanding the definition above, two independent occurrences of R°, taken together with their intervening atom(s), form a 3–12-membered saturated, partially unsaturated, or aryl mono- or bicyclic ring having 0–4 heteroatoms independently selected from nitrogen, oxygen, or sulfur, which may be substituted as defined below.

[0032] Suitable monovalent substituents on R° (or the ring formed by taking two independent occurrences of R° together with their intervening atoms), are independently halogen, -(CH$_2$)$_{0-2}$R$^\bullet$, -(haloR$^\bullet$), -(CH$_2$)$_{0-2}$OH, -(CH$_2$)$_{0-2}$OR$^\bullet$, -(CH$_2$)$_{0-2}$CH(OR$^\bullet$)$_2$; -O(haloR$^\bullet$), -CN, -N$_3$, -(CH$_2$)$_{0-2}$C(O)R$^\bullet$, -(CH$_2$)$_{0-2}$C(O)OH, -(CH$_2$)$_{0-2}$C(O)OR$^\bullet$, -(CH$_2$)$_{0-2}$SR$^\bullet$, -(CH$_2$)$_{0-2}$SH, -(CH$_2$)$_{0-2}$NH$_2$, -(CH$_2$)$_{0-2}$NHR$^\bullet$, -(CH$_2$)$_{0-2}$NR$^\bullet_2$, -NO$_2$, -SiR$^\bullet_3$, -OSiR$^\bullet_3$, -C(O)SR$^\bullet$, -(C$_{1-4}$ straight or branched alkylene)C(O)OR$^\bullet$, or -SSR$^\bullet$ wherein each R$^\bullet$ is unsubstituted or where preceded by "halo" is substituted only with one or more halogens, and is independently selected from C$_{1-4}$ aliphatic, -CH$_2$Ph, -O(CH$_2$)$_{0-1}$Ph, or a 5–6-membered saturated, partially unsaturated, or aryl ring having 0–4 heteroatoms independently selected from nitrogen, oxygen, or sulfur. Suitable divalent substituents on a saturated carbon atom of R° include =O and =S.

[0033] Suitable divalent substituents on a saturated carbon atom of an "optionally substituted" group include the following: =O, =S, =NNR$^*_2$, =NNHC(O)R*, =NNHC(O)OR*, =NNHS(O)$_2$R*, =NR*, =NOR*, –O(C(R$^*_2$))$_{2-3}$O–, or –S(C(R$^*_2$))$_{2-3}$S–, wherein each independent occurrence of R* is selected from hydrogen, C$_{1-6}$ aliphatic which may be substituted as defined below, or an unsubstituted 5–6-membered saturated, partially unsaturated, or aryl ring having 0–4 heteroatoms independently selected from nitrogen, oxygen, or sulfur. Suitable divalent

substituents that are bound to vicinal substitutable carbons of an "optionally substituted" group include: $-O(CR^*_2)_{2-3}O-$, wherein each independent occurrence of R^* is selected from hydrogen, C_{1-6} aliphatic which may be substituted as defined below, or an unsubstituted 5–6-membered saturated, partially unsaturated, or aryl ring having 0–4 heteroatoms independently selected from nitrogen, oxygen, or sulfur.

[0034] Suitable substituents on the aliphatic group of R^* include halogen, $-R^\bullet$, -(haloR$^\bullet$), -OH, $-OR^\bullet$, -O(haloR$^\bullet$), -CN, -C(O)OH, $-C(O)OR^\bullet$, $-NH_2$, $-NHR^\bullet$, $-NR^\bullet_2$, or $-NO_2$, wherein each $R^\bullet$ is unsubstituted or where preceded by "halo" is substituted only with one or more halogens, and is independently C_{1-4} aliphatic, $-CH_2Ph$, $-O(CH_2)_{0-1}Ph$, or a 5–6-membered saturated, partially unsaturated, or aryl ring having 0–4 heteroatoms independently selected from nitrogen, oxygen, or sulfur.

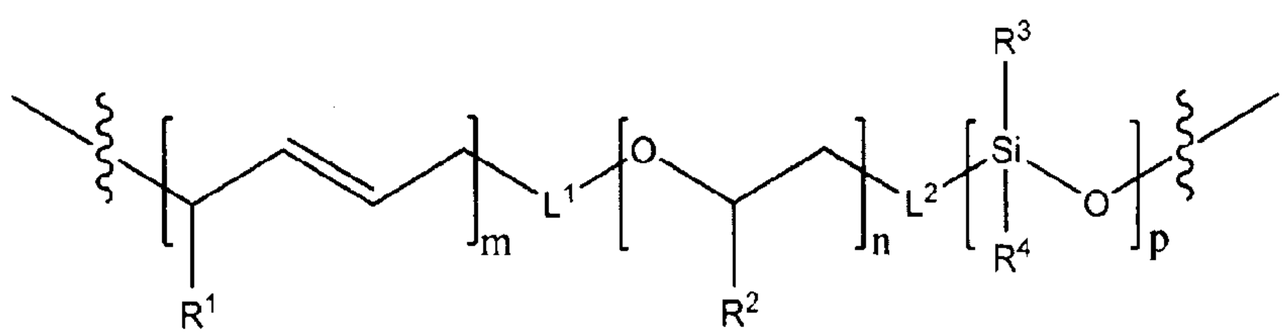
[0035] Suitable substituents on a substitutable nitrogen of an "optionally substituted" group include $-R^\dagger$, $-NR^\dagger_2$, $-C(O)R^\dagger$, $-C(O)OR^\dagger$, $-C(O)C(O)R^\dagger$, $-C(O)CH_2C(O)R^\dagger$, $-S(O)_2R^\dagger$, $-S(O)_2NR^\dagger_2$, $-C(S)NR^\dagger_2$, $-C(NH)NR^\dagger_2$, or $-N(R^\dagger)S(O)_2R^\dagger$; wherein each $R^\dagger$ is independently hydrogen, C_{1-6} aliphatic which may be substituted as defined below, unsubstituted -OPh, or an unsubstituted 5–6-membered saturated, partially unsaturated, or aryl ring having 0–4 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or, notwithstanding the definition above, two independent occurrences of $R^\dagger$, taken together with their intervening atom(s) form an unsubstituted 3–12-membered saturated, partially unsaturated, or aryl mono- or bicyclic ring having 0–4 heteroatoms independently selected from nitrogen, oxygen, or sulfur.

[0036] Suitable substituents on the aliphatic group of $R^\dagger$ are independently halogen, $-R^\bullet$, -(haloR$^\bullet$), -OH, $-OR^\bullet$, -O(haloR$^\bullet$), -CN, -C(O)OH, $-C(O)OR^\bullet$, $-NH_2$, $-NHR^\bullet$, $-NR^\bullet_2$, or $-NO_2$, wherein each $R^\bullet$ is unsubstituted or where preceded by "halo" is substituted only with one or more halogens, and is independently C_{1-4} aliphatic, $-CH_2Ph$, $-O(CH_2)_{0-1}Ph$, or a 5–6-membered saturated, partially unsaturated, or aryl ring having 0–4 heteroatoms independently selected from nitrogen, oxygen, or sulfur.

3. *Description of Exemplary Embodiments:*

A. *Multiblock Copolymers*

[0037] As described generally above, one embodiment of the present invention provides a triblock copolymer of formula [polybutadiene][polyalkyl ether][polysiloxane]. In certain embodiments, a provided triblock copolymer is of formula **I**:



I

wherein the copolymers are chemically interspersed (bound) between urethane and/or urea linkages (i.e., at the bond designated with $\S$) and wherein each of m, n, p, L^1, L^2, R^1, R^2, R^3, and R^4 is as defined and described herein.

[0038] In certain embodiments, m and p are each independently between 2 and 50 and n is between 2 and 20. In some embodiments, m and p are each independently between 2 and 30 and n is between 2 and 20. In certain embodiments, each of m, n, and p are independently from 8 to 16.

[0039] As defined generally above, each of R^1, R^2, R^3, and R^4 is independently selected from one or more of halogen, R, OR, $-CO_2R$, a fluorinated hydrocarbon, a polyether, a polyester or a fluoropolymer. In some embodiments, one or more of R^1, R^2, R^3, R^4, R^5 and R^6 is $-CO_2R$. In some embodiments, one or more of R^1, R^2, R^3, R^4, R^5 and R^6 is $-CO_2R$ wherein each R is independently an optionally substituted C_{1-6} aliphatic group. In certain embodiments, one or more of R^1, R^2, R^3, and R^4 is $-CO_2R$ wherein each R is independently an unsubstituted C_{1-6} alkyl group. Exemplary such groups include methanoic or ethanoic acid as well as methacrylic acid and other acrylic acids.

[0040] In certain embodiments, one or more of R^1, R^2, R^3, and R^4 is independently R. In some embodiments, one or more of R^1, R^2, R^3, and R^4 is an optionally substituted C_{1-6} aliphatic group. In certain embodiments, one or more of R^1, R^2, R^3, and R^4 is an optionally substituted C_{1-6} alkyl. In other embodiments, one or more of R^1, R^2, R^3, and R^4 is an optionally substituted group selected from phenyl, 8-10 membered bicyclic aryl, a 4-8 membered monocyclic saturated or partially unsaturated heterocyclic ring having 1-2 heteroatoms independently selected from nitrogen, oxygen, or sulphur, or 5-6 membered monocyclic or 8-10 membered bicyclic

heteroaryl group having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulphur. Exemplary such R^1, R^2, R^3, and R^4 groups include methyl, ethyl, propyl, isopropyl, cyclopropyl, butyl, isobutyl, cyclobutyl, phenyl, pyridyl, morpholinyl, pyrrolidinyl, imidazolyl, and cyclohexyl. In certain embodiments, one or more of R^1, R^2, R^3, and R^4 is methyl, ethyl, propyl, or a higher homolog. In certain embodiments, R^2 is methyl, ethyl, propyl, or a higher homolog due to the relative hydrophobicity conferred on the polymer chain. Particularly preferred is R^2 being methyl.

[0041] In certain embodiments, one or more of R^1, R^2, R^3, and R^4 is independently -OR. In some embodiments, one or more of R^1, R^2, R^3, and R^4 is –OR wherein R is an optionally substituted C_{1-6} aliphatic group. In certain embodiments, one or more of R^1, R^2, R^3, and R^4 is –OR wherein R is C_{1-6} alkyl. In other embodiments, one or more of R^1, R^2, R^3, and R^4 is–OR wherein R is an optionally substituted group selected from phenyl, 8-10 membered bicyclic aryl, a 4-8 membered monocyclic saturated or partially unsaturated heterocyclic ring having 1-2 heteroatoms independently selected from nitrogen, oxygen, or sulphur, or 5-6 membered monocyclic or 8-10 membered bicyclic heteroaryl group having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulphur. Exemplary such R^1, R^2, R^3, R^4, R^5 and R^6 groups include -Omethyl, -Oethyl, -Opropyl, -Oisopropyl, -Ocyclopropyl, -Obutyl, -Oisobutyl, -Ocyclobutyl, -Ophenyl, -Opyridyl, -Omorpholinyl, -Opyrrolidinyl, -Oimidazolyl, and -Ocyclohexyl.

[0042] In certain embodiments, one or more of R^1, R^2, R^3, and R^4 is independently R wherein each R is a C_{1-6} aliphatic group substituted with one or more halogens. In some embodiments, each R is C_{1-6} aliphatic substituted with one, two, or three halogens. In other embodiments, each R is a perfluorinated C_{1-6} aliphatic group. Examples of fluorinated hydrocarbons represented by R^1, R^2, R^3, and R^4 include mono-, di-, tri, or perfluorinated methyl, ethyl, propyl, butyl, or phenyl. In some embodiments, each of R^1, R^2, R^3, and R^4 is trifluoromethyl, trifluoroethyl, or trifluoropropyl.

[0043] In certain embodiments, one or more of R^1, R^2, R^3, and R^4 is independently a polyether. Examples of polyethers represented by R^1, R^2, R^3, and R^4 include poly(ethylene oxide), poly(difluoromethyl ethylene oxide), poly(trifluoromethyl ethylene oxide), poly(propylene oxide), poly(difluoromethyl propylene oxide), poly(propylene oxide), poly(trifluoromethyl propylene oxide), poly(butylene oxide), poly(tetramethylene ether glycol),

poly(tetrahydrofuran), poly(oxymethylene), poly(ether ketone), poly(etherether ketone) and copolymers thereof.

[0044] In certain embodiments, one or more of R^1, R^2, R^3, R^4, R^5 and R^6 is independently a polyester. Examples of polyesters represented by R^1, R^2, R^3, R^4, R^5 and R^6 include poly(ethylene terephthalate) (PET), poly(ethylene terephthalate ionomer) (PETI), poly(ethylene naphthalate) (PEN), poly(methylene naphthalate) (PTN), poly(butylene teraphalate) (PBT), poly(butylene naphthalate) (PBN), polycarbonate.

[0045] In certain embodiments, one or more of R^1, R^2, R^3, R^4, R^5 and R^6 is independently a fluoropolymer. Examples of fluoropolymers represented by R^1, R^2, R^3, R^4, R^5 and R^6 include poly(tetrafluoroethylene), poly(methyl di-fluoroethyl siloxane), poly(methyl tri-fluoroethyl siloxane), poly(phenyl di-fluoroethyl siloxane).

[0046] In some embodiments, R^1, R^2, R^3, and R^4 is independently hydrogen, hydroxyl, carboxylic acids such as methanoic or ethanoic acid as well as methacrylic acid and other acrylic acids. Alkyl or aryl hydrocarbons such as methyl, ethyl, propyl, butyl, phenyl and ethers thereof. Fluorinated hydrocarbons such as mono-, di-, tri, or perfluorinated methyl, ethyl, propyl, butyl, phenyl. Polyether such as Poly(ethylene oxide), poly(difluoromethyl ethylene oxide), poly(trifluoromethyl ethylene oxide), poly(propylene oxide), poly(difluoromethyl propylene oxide), poly(propylene oxide), poly(trifluoromethyl propylene oxide), poly(butylene oxide), poly(tetramethylene ether glycol), poly(tetrahydrofuran), poly(oxymethylene), poly(ether ketone), poly(etherether ketone) and copolymers thereof. Polyesters such as Poly(ethylene terephthalate) (PET), poly(ethylene terephthalate ionomer) (PETI), poly(ethylene naphthalate) (PEN), poly(methylene naphthalate) (PTN), Poly(Butylene Teraphalate) (PBT), poly(butylene naphthalate) (PBN), polycarbonate and .fluoropolymer such as Poly(tetrafluoroethylene), poly(methyl di-fluoroethyl siloxane), poly(methyl tri-fluoroethyl siloxane), poly(phenyl di-fluoroethyl siloxane).

[0047] In some embodiments, R^1 is hydrogen. In some embodiments, R^1 is halogen. In certain embodiments, R^1 is chloro or fluoro. In some embodiments, R^1 is an optionally substituted C_{1-6} alkyl. In certain embodiments, R^1 is methyl.

[0048] In some embodiments, R^2 is hydrogen. In some embodiments, R^2 is an optionally substituted C_{1-6} alkyl. In certain embodiments, R^2 is methyl, ethyl, propyl, or a higher homolog

due to the relative hydrophobicity conferred on the polymer chain. Particularly preferred is R^2 being methyl.

[0049] In some embodiments, R^3 is an optionally substituted C_{1-6} alkyl. In certain embodiments, R^3 is methyl. In certain embodiments, R^3 is $-CH_2CH_2F$. In some embodiments, R^3 is halogen. In certain embodiments, R^3 is fluoro. In some embodiments, R^3 is phenyl.

[0050] In some embodiments, R^4 is an optionally substituted C_{1-6} alkyl. In certain embodiments, R^4 is methyl. In certain embodiments, R^4 is $-CH_2CH_2F$. In some embodiments, R^4 is halogen. In certain embodiments, R^4 is fluoro. In some embodiments, R^4 is phenyl

[0051] As defined generally above, each of L^1 and L^2 is independently a bivalent C_{1-20} hydrocarbon chain wherein 1-4 methylene units of the hydrocarbon chain are optionally and independently replaced by –O-, -S-, -NHC(O)O-, -NHC(O)NH-, -N(R)-, -C(O)-, -C(O)N(R)-, -N(R)C(O)-, -SO2-, -SO2N(R)-, -N(R)SO2-, -OC(O)-, –C(O)O-, or a bivalent cycloalkylene, arylene, heterocyclene, or heteroarylene. In some embodiments, each of L^1 and L^2 is independently a bivalent C_{1-20} alkylene chain. In certain embodiments, each of L^1 and L^2 is independently a bivalent C_{1-10} alkylene chain. In certain embodiments, each of L^1 and L^2 is independently a bivalent C_{1-6} alkylene chain. In certain embodiments, each of L^1 and L^2 is independently a bivalent C_{1-4} alkylene chain. Exemplary such L^1 and L^2 groups include methylene, ethylene, propylene, butylene or higher bivalent alkanes.

[0052] In some embodiments, each of L^1 and L^2 is independently a bivalent C_{1-20} alkylene chain wherein one methylene unit of the chain is replaced by –O-. In some embodiments, each of L^1 and L^2 is independently a bivalent C_{1-10} alkylene chain wherein one methylene unit of the chain is replaced by –O-. In some embodiments, each of L^1 and L^2 is independently a bivalent C_{1-6} alkylene chain wherein one methylene unit of the chain is replaced by –O-. In some embodiments, each of L^1 and L^2 is independently a bivalent C_{1-4} alkylene chain wherein one methylene unit of the chain is replaced by –O-. Exemplary such L^1 and L^2 groups include $-OCH_2-$, $-OCH_2CH_2-$, $-OCH_2CH_2CH_2-$, $-OCH_2CH_2CH_2CH_2-$, or higher bivalent alkylene ethers.

[0053] In some embodiments, each of L^1 and L^2 is independently a bivalent C_{1-20} alkylene chain wherein at least one methylene unit of the chain is replaced by –O- and at least one methylene unit of the chain is replaced by a bivalent arylene. In some embodiments, each of L^1 and L^2 is independently a bivalent C_{1-10} alkylene chain wherein at least one methylene unit of the chain is replaced by –O- and at least one methylene unit of the chain is replaced by a bivalent

arylene. In some embodiments, each of L^1 and L^2 is independently a bivalent C_{1-6} alkylene chain wherein at least one methylene unit of the chain is replaced by –O- and at least one methylene unit of the chain is replaced by a bivalent arylene. In some embodiments, each of L^1 and L^2 is independently a bivalent C_{1-4} alkylene chain wherein at least one methylene unit of the chain is replaced by –O- and at least one methylene unit of the chain is replaced by a bivalent arylene. Exemplary such L^1 and L^2 groups include -OCH_2-phenylene-, -OCH_2CH_2-phenylene-, -OCH_2CH_2-phenylene-CH_2-, -$OCH_2CH_2CH_2CH_2$--phenylene-, and the like.

[0054] In some embodiments, each of L^1 and L^2 is independently a bivalent C_{1-20} alkylene chain wherein three methylene units of the chain are replaced by –N(R)C(O)N(R)-, -N(R)C(O)O-, or -OC(O)N(R)-. In some embodiments, each of L^1 and L^2 is independently a bivalent C_{1-10} alkylene chain wherein one methylene unit of the chain is replaced by –O-. In some embodiments, each of L^1 and L^2 is independently a bivalent C_{1-6} alkylene chain wherein one methylene unit of the chain are replaced by –N(R)C(O)N(R)-, -N(R)C(O)O-, or -OC(O)N(R)-. In some embodiments, each of L^1 and L^2 is independently a bivalent C_{1-4} alkylene chain wherein one methylene unit of the chain are replaced by –N(R)C(O)N(R)-, -N(R)C(O)O-, or -OC(O)N(R)-. Exemplary such L^1 and L^2 groups include –N(H)C(O)N(H)-, -N(H)C(O)O-, and -OC(O)N(H)-.

[0055] In some embodiments, L^1 is a urethane. In some embodiments, L^2 is –CH_2CH_2-.

[0056] In some embodiments, R^1 and R^2 is methyl. In some embodiments, one or both of R^3 and R^4 is independently a C_{1-20} hydrocarbon chain wherein 1-4 methylene units of the hydrocarbon chain are optionally and independently substituted by halogen. In some embodiments, R^3 is a C_{1-20} hydrocarbon chain wherein 1-4 methylene units of the hydrocarbon chain are optionally and independently substituted by halogen. In some embodiments, R^4 is a C_{1-20} hydrocarbon chain wherein 1-4 methylene units of the hydrocarbon chain are optionally and independently substituted by halogen. In some embodiments, R^3 and R^4 are independently a C_{1-20} hydrocarbon chain wherein 1-4 methylene units of the hydrocarbon chain are optionally and independently substituted by halogen. In some embodiments, one or both of R^3 and R^4 is independently a C_{1-20} hydrocarbon chain. In some embodiments, R^3 is a C_{1-20} hydrocarbon chain. In some embodiments, R^4 is a C_{1-20} hydrocarbon chain. In some embodiments, R^3 and R^4 are independently a C_{1-20} hydrocarbon chain. In some embodiments, L^1 and L^2 are independently a bivalent C_{1-20} hydrocarbon chain wherein 1-4 methylene units of the hydrocarbon chain are

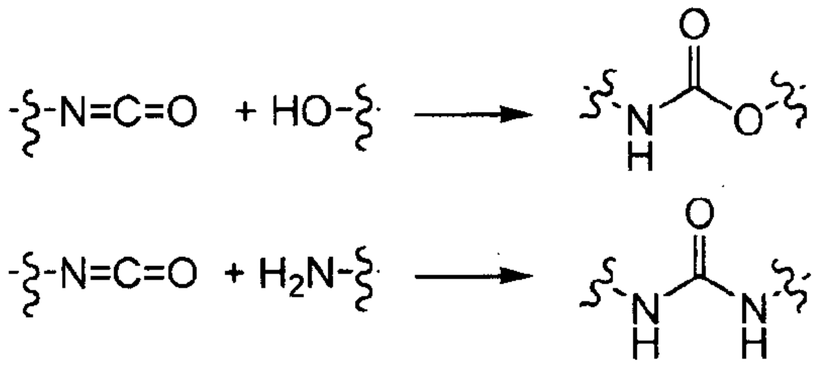
optionally and independently replaced by –NHC(O)O- or –NHC(O)NH-. In some embodiments, L^1 is –NHC(O)O- or –NHC(O)NH-. In some embodiments, L^2 is a C_{1-20} hydrocarbon chain.

[0057] In some embodiments, R^1 and R^2 are methyl, one or both of R^3 and R^4 is independently a C_{1-20} hydrocarbon chain wherein 1-4 methylene units of the hydrocarbon chain are optionally and independently substituted by halogen, and L^1 and L^2 are independently a bivalent C_{1-20} hydrocarbon chain wherein 1-4 methylene units of the hydrocarbon chain are optionally and independently replaced by –NHC(O)O- or –NHC(O)NH-.

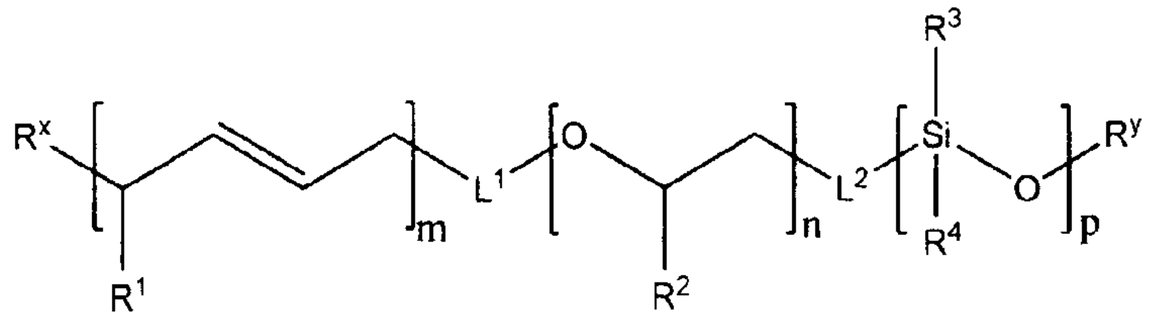
[0058] In some embodiments, R^1 and R^2 are methyl, one or both of R^3 and R^4 is independently a C_{1-20} hydrocarbon chain wherein 1-4 methylene units of the hydrocarbon chain are optionally and independently substituted by halogen, L^1 is –NHC(O)O- or –NHC(O)NH-, and L^2 is a C_{1-20} hydrocarbon chain.

[0059] In some embodiments, R^1 and R^2 are methyl, one or both of R^3 and R^4 is independently a C_{1-20} hydrocarbon chain, L^1 is –NHC(O)O- or –NHC(O)NH-, and L^2 is a C_{1-20} hydrocarbon chain.

[0060] One of ordinary skill in the art would understand that a polyurethane results from the reaction of an isocyanate and a hydroxyl group. Similarly, a polyurea results from the reaction of an isocyanate and an amine. Each of these reactions is depicted below.



[0061] Thus, it is readily apparent that provided compounds of formula **I** can be functionalized with end groups suitable for forming urethane and/or urea linkages. In certain embodiments, the present invention provides a compound of formula **II**:



II

wherein:

each of R^x and R^y is independently –OH, -NH_2, a protected hydroxyl or a protected amine;

each of R^1, R^2, R^3, and R^4 is independently selected from one or more of halogen, R, OR, -CO_2R, a fluorinated hydrocarbon, a polyether, a polyester or a fluoropolymer;

each R is independently hydrogen, an optionally substituted C_{1-20} aliphatic group, or an optionally substituted group selected from phenyl, 8-10 membered bicyclic aryl, a 4-8 membered monocyclic saturated or partially unsaturated heterocyclic ring having 1-2 heteroatoms independently selected from nitrogen, oxygen, or sulphur, or 5-6 membered monocyclic or 8-10 membered bicyclic heteroaryl group having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

each of m, n, and p is independently 2 to 100; and

each of L^1 and L^2 is independently a bivalent C_{1-20} hydrocarbon chain wherein 1-4 methylene units of the hydrocarbon chain are optionally and independently replaced by –O-, -S-, -N(R)C(O)O-, -N(R)C(O)N(R)-, -OC(O)N(R)-, -N(R)-, -C(O)-, -C(O)N(R)-, -N(R)C(O)-, -SO2-, -SO2N(R)-, -N(R)SO2-, -OC(O)-, –C(O)O-, or a bivalent cycloalkylene, arylene, heterocyclene, or heteroarylene.

[0062] In some embodiments, each of m, n, p, L^1, L^2, R^1, R^2, R^3, and R^4 is as defined and described herein.

[0063] As defined generally above, each of R^x and R^y is independently –OH, -NH_2, a protected hydroxyl or a protected amine. In some embodiments, both of R^x and R^y are –OH. In other embodiments, both of R^x and R^y are –NH_2. In some embodiments one of R^x and R^y is –OH and the other is –NH_2.

[0064] In some embodiments, each of R^x and R^y is independently a protected hydroxyl or a protected amine. Such protected hydroxyl and protected amine groups are well known to one of skill in the art and include those described in detail in *Protecting Groups in Organic Synthesis*, T. W. Greene and P. G. M. Wuts, 3rd edition, John Wiley & Sons, 1999.

Exemplary protected amines include methyl carbamate, ethyl carbamante, 9–fluorenylmethyl carbamate (Fmoc), 9–(2–sulfo)fluorenylmethyl carbamate, 9–(2,7–dibromo)fluoroenylmethyl carbamate, 2,7–di–t–butyl–[9–(10,10–dioxo–10,10,10,10–tetrahydrothioxanthyl)]methyl carbamate (DBD–Tmoc), 4–methoxyphenacyl carbamate (Phenoc), 2,2,2–trichloroethyl carbamate (Troc), 2–trimethylsilylethyl carbamate (Teoc), 2–

phenylethyl carbamate (hZ), 1–(1–adamantyl)–1–methylethyl carbamate (Adpoc), 1,1–dimethyl–2–haloethyl carbamate, 1,1–dimethyl–2,2–dibromoethyl carbamate (DB–t–BOC), 1,1–dimethyl–2,2,2–trichloroethyl carbamate (TCBOC), 1–methyl–1–(4–biphenylyl)ethyl carbamate (Bpoc), 1–(3,5–di–t–butylphenyl)–1–methylethyl carbamate (t–Bumeoc), 2–(2' and 4'–pyridyl)ethyl carbamate (Pyoc), 2–(N,N–dicyclohexylcarboxamido)ethyl carbamate, t–butyl carbamate (BOC), 1–adamantyl carbamate (Adoc), vinyl carbamate (Voc), allyl carbamate (Alloc), 1–isopropylallyl carbamate (Ipaoc), cinnamyl carbamate (Coc), 4–nitrocinnamyl carbamate (Noc), 8–quinolyl carbamate, N–hydroxypiperidinyl carbamate, alkyldithio carbamate, benzyl carbamate (Cbz), p–methoxybenzyl carbamate (Moz), p–nitobenzyl carbamate, p–bromobenzyl carbamate, p–chlorobenzyl carbamate, 2,4–dichlorobenzyl carbamate, 4–methylsulfinylbenzyl carbamate (Msz), 9–anthrylmethyl carbamate, diphenylmethyl carbamate, 2–methylthioethyl carbamate, 2–methylsulfonylethyl carbamate, 2–(p–toluenesulfonyl)ethyl carbamate, [2–(1,3–dithianyl)]methyl carbamate (Dmoc), 4–methylthiophenyl carbamate (Mtpc), 2,4–dimethylthiophenyl carbamate (Bmpc), 2–phosphonioethyl carbamate (Peoc), 2–triphenylphosphonioisopropyl carbamate (Ppoc), 1,1–dimethyl–2–cyanoethyl carbamate, m–chloro–p–acyloxybenzyl carbamate, p–(dihydroxyboryl)benzyl carbamate, 5–benzisoxazolylmethyl carbamate, 2–(trifluoromethyl)–6–chromonylmethyl carbamate (Tcroc), m–nitrophenyl carbamate, 3,5–dimethoxybenzyl carbamate, o–nitrobenzyl carbamate, 3,4–dimethoxy–6–nitrobenzyl carbamate, phenyl(o–nitrophenyl)methyl carbamate, phenothiazinyl–(10)–carbonyl derivative, N'–p–toluenesulfonylaminocarbonyl derivative, N'–phenylaminothiocarbonyl derivative, t–amyl carbamate, S–benzyl thiocarbamate, p–cyanobenzyl carbamate, cyclobutyl carbamate, cyclohexyl carbamate, cyclopentyl carbamate, cyclopropylmethyl carbamate, p–decyloxybenzyl carbamate, 2,2–dimethoxycarbonylvinyl carbamate, o–(N,N–dimethylcarboxamido)benzyl carbamate, 1,1–dimethyl–3–(N,N–dimethylcarboxamido)propyl carbamate, 1,1–dimethylpropynyl carbamate, di(2–pyridyl)methyl carbamate, 2–furanylmethyl carbamate, 2–iodoethyl carbamate, isoborynl carbamate, isobutyl carbamate, isonicotinyl carbamate, p–(p'–methoxyphenylazo)benzyl carbamate, 1–methylcyclobutyl carbamate, 1–methylcyclohexyl carbamate, 1–methyl–1–cyclopropylmethyl carbamate, 1–methyl–1–(3,5–dimethoxyphenyl)ethyl carbamate, 1–methyl–1–(p–phenylazophenyl)ethyl carbamate, 1–methyl–1–phenylethyl carbamate, 1–methyl–1–(4–pyridyl)ethyl carbamate, phenyl carbamate, p–(phenylazo)benzyl carbamate, 2,4,6–tri–t–

butylphenyl carbamate, 4–(trimethylammonium)benzyl carbamate, 2,4,6–trimethylbenzyl carbamate, formamide, acetamide, chloroacetamide, trichloroacetamide, trifluoroacetamide, phenylacetamide, 3–phenylpropanamide, picolinamide, 3–pyridylcarboxamide, N–benzoylphenylalanyl derivative, benzamide, p–phenylbenzamide, o–nitophenylacetamide, o–nitrophenoxyacetamide, acetoacetamide, (N'–dithiobenzyloxycarbonylamino)acetamide, 3–(p–hydroxyphenyl)propanamide, 3–(o–nitrophenyl)propanamide, 2–methyl–2–(o–nitrophenoxy)propanamide, 2–methyl–2–(o–phenylazophenoxy)propanamide, 4–chlorobutanamide, 3–methyl–3–nitrobutanamide, o–nitrocinnamide, N–acetylmethionine derivative, o–nitrobenzamide, o–(benzoyloxymethyl)benzamide, 4,5–diphenyl–3–oxazolin–2–one, N–phthalimide, N–dithiasuccinimide (Dts), N–2,3–diphenylmaleimide, N–2,5–dimethylpyrrole, N–1,1,4,4–tetramethyldisilylazacyclopentane adduct (STABASE), 5–substituted 1,3–dimethyl–1,3,5–triazacyclohexan–2–one, 5–substituted 1,3–dibenzyl–1,3,5–triazacyclohexan–2–one, 1–substituted 3,5–dinitro–4–pyridone, N–methylamine, N–allylamine, N–[2–(trimethylsilyl)ethoxy]methylamine (SEM), N–3–acetoxypropylamine, N–(1–isopropyl–4–nitro–2–oxo–3–pyroolin–3–yl)amine, quaternary ammonium salts, N–benzylamine, N–di(4–methoxyphenyl)methylamine, N–5–dibenzosuberylamine, N–triphenylmethylamine (Tr), N–[(4–methoxyphenyl)diphenylmethyl]amine (MMTr), N–9–phenylfluorenylamine (PhF), N–2,7–dichloro–9–fluorenylmethyleneamine, N–ferrocenylmethylamino (Fcm), N–2–picolylamino N'–oxide, N–1,1–dimethylthiomethyleneamine, N–benzylideneamine, N–p–methoxybenzylideneamine, N–diphenylmethyleneamine, N–[(2–pyridyl)mesityl]methyleneamine, N–(N',N'–dimethylaminomethylene)amine, N,N'–isopropylidenediamine, N–p–nitrobenzylideneamine, N–salicylideneamine, N–5–chlorosalicylideneamine, N–(5–chloro–2–hydroxyphenyl)phenylmethyleneamine, N–cyclohexylideneamine, N–(5,5–dimethyl–3–oxo–1–cyclohexenyl)amine, N–borane derivative, N–diphenylborinic acid derivative, N–[phenyl(pentacarbonylchromium– or tungsten)carbonyl]amine, N–copper chelate, N–zinc chelate, N–nitroamine, N–nitrosoamine, amine N–oxide, diphenylphosphinamide (Dpp), dimethylthiophosphinamide (Mpt), diphenylthiophosphinamide (Ppt), dialkyl phosphoramidates, dibenzyl phosphoramidate, diphenyl phosphoramidate, benzenesulfenamide, o–nitrobenzenesulfenamide (Nps), 2,4–dinitrobenzenesulfenamide, pentachlorobenzenesulfenamide, 2–nitro–4–methoxybenzenesulfenamide, triphenylmethylsulfenamide, 3–nitropyridinesulfenamide (Npys),

p–toluenesulfonamide (Ts), benzenesulfonamide, 2,3,6,–trimethyl–4–methoxybenzenesulfonamide (Mtr), 2,4,6–trimethoxybenzenesulfonamide (Mtb), 2,6–dimethyl–4–methoxybenzenesulfonamide (Pme), 2,3,5,6–tetramethyl–4–methoxybenzenesulfonamide (Mte), 4–methoxybenzenesulfonamide (Mbs), 2,4,6–trimethylbenzenesulfonamide (Mts), 2,6–dimethoxy–4–methylbenzenesulfonamide (iMds), 2,2,5,7,8–pentamethylchroman–6–sulfonamide (Pmc), methanesulfonamide (Ms), β–trimethylsilylethanesulfonamide (SES), 9–anthracenesulfonamide, 4–(4',8'–dimethoxynaphthylmethyl)benzenesulfonamide (DNMBS), benzylsulfonamide, trifluoromethylsulfonamide, and phenacylsulfonamide.

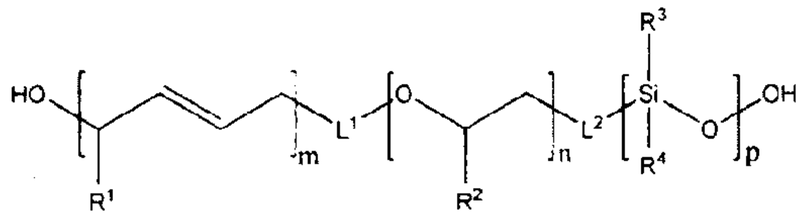
[0065] Exemplary hydroxyl protecting groups include methyl, methoxylmethyl (MOM), methylthiomethyl (MTM), t–butylthiomethyl, (phenyldimethylsilyl)methoxymethyl (SMOM), benzyloxymethyl (BOM), p–methoxybenzyloxymethyl (PMBM), (4–methoxyphenoxy)methyl (p–AOM), guaiacolmethyl (GUM), t–butoxymethyl, 4–pentenyloxymethyl (POM), siloxymethyl, 2–methoxyethoxymethyl (MEM), 2,2,2–trichloroethoxymethyl, bis(2–chloroethoxy)methyl, 2–(trimethylsilyl)ethoxymethyl (SEMOR), tetrahydropyranyl (THP), 3–bromotetrahydropyranyl, tetrahydrothiopyranyl, 1 methoxycyclohexyl, 4–methoxytetrahydropyranyl (MTHP), 4–methoxytetrahydrothiopyranyl, 4–methoxytetrahydrothiopyranyl S,S–dioxide, 1–[(2–chloro–4–methyl)phenyl]–4–methoxypiperidin–4–yl (CTMP), 1,4–dioxan–2–yl, tetrahydrofuranyl, tetrahydrothiofuranyl, 2,3,3a,4,5,6,7,7a–octahydro–7,8,8–trimethyl–4,7–methanobenzofuran–2–yl, 1–ethoxyethyl, 1–(2–chloroethoxy)ethyl, 1–methyl–1–methoxyethyl, 1–methyl–1–benzyloxyethyl, 1–methyl–1–benzyloxy–2–fluoroethyl, 2,2,2–trichloroethyl, 2–trimethylsilylethyl, 2–(phenylselenyl)ethyl, t–butyl, allyl, p–chlorophenyl, p–methoxyphenyl, 2,4–dinitrophenyl, benzyl, p–methoxybenzyl, 3,4–dimethoxybenzyl, o–nitrobenzyl, p–nitrobenzyl, p–halobenzyl, 2,6–dichlorobenzyl, p–cyanobenzyl, p–phenylbenzyl, 2–picolyl, 4–picolyl, 3–methyl–2–picolyl N–oxido, diphenylmethyl, p,p'–dinitrobenzhydryl, 5–dibenzosuberyl, triphenylmethyl, α–naphthyldiphenylmethyl, p–methoxyphenyldiphenylmethyl, di(p–methoxyphenyl)phenylmethyl, tri(p–methoxyphenyl)methyl, 4–(4'–bromophenacyloxyphenyl)diphenylmethyl, 4,4',4''–tris(4,5–dichlorophthalimidophenyl)methyl, 4,4',4''–tris(levulinoyloxyphenyl)methyl, 4,4',4''–tris(benzoyloxyphenyl)methyl, 3–(imidazol–1–yl)bis(4',4''–dimethoxyphenyl)methyl, 1,1–bis(4–methoxyphenyl)–1'–pyrenylmethyl, 9–anthryl, 9–(9–phenyl)xanthenyl, 9–(9–phenyl–10–oxo)anthryl, 1,3–benzodithiolan–2–yl, benzisothiazolyl S,S–dioxido, trimethylsilyl (TMS),

triethylsilyl (TES), triisopropylsilyl (TIPS), dimethylisopropylsilyl (IPDMS), diethylisopropylsilyl (DEIPS), dimethylthexylsilyl, t–butyldimethylsilyl (TBDMS), t–butyldiphenylsilyl (TBDPS), tribenzylsilyl, tri–p–xylylsilyl, triphenylsilyl, diphenylmethylsilyl (DPMS), t–butylmethoxyphenylsilyl (TBMPS), formate, benzoylformate, acetate, chloroacetate, dichloroacetate, trichloroacetate, trifluoroacetate, methoxyacetate, triphenylmethoxyacetate, phenoxyacetate, p–chlorophenoxyacetate, 3–phenylpropionate, 4–oxopentanoate (levulinate), 4,4–(ethylenedithio)pentanoate (levulinoyldithioacetal), pivaloate, adamantoate, crotonate, 4–methoxycrotonate, benzoate, p–phenylbenzoate, 2,4,6–trimethylbenzoate (mesitoate), alkyl methyl carbonate, 9–fluorenylmethyl carbonate (Fmoc), alkyl ethyl carbonate, alkyl 2,2,2–trichloroethyl carbonate (Troc), 2–(trimethylsilyl)ethyl carbonate (TMSEC), 2–(phenylsulfonyl) ethyl carbonate (Psec), 2–(triphenylphosphonio) ethyl carbonate (Peoc), alkyl isobutyl carbonate, alkyl vinyl carbonate alkyl allyl carbonate, alkyl p–nitrophenyl carbonate, alkyl benzyl carbonate, alkyl p–methoxybenzyl carbonate, alkyl 3,4–dimethoxybenzyl carbonate, alkyl o–nitrobenzyl carbonate, alkyl p–nitrobenzyl carbonate, alkyl S–benzyl thiocarbonate, 4–ethoxy–1–napthhyl carbonate, methyl dithiocarbonate, 2–iodobenzoate, 4–azidobutyrate, 4–nitro–4–methylpentanoate, o–(dibromomethyl)benzoate, 2–formylbenzenesulfonate, 2–(methylthiomethoxy)ethyl, 4–(methylthiomethoxy)butyrate, 2–(methylthiomethoxymethyl)benzoate, 2,6–dichloro–4–methylphenoxyacetate, 2,6–dichloro–4–(1,1,3,3–tetramethylbutyl)phenoxyacetate, 2,4–bis(1,1–dimethylpropyl)phenoxyacetate, chlorodiphenylacetate, isobutyrate, monosuccinoate, (E)–2–methyl–2–butenoate, o–(methoxycarbonyl)benzoate, α–naphthoate, nitrate, alkyl N,N,N',N'–tetramethylphosphorodiamidate, alkyl N–phenylcarbamate, borate, dimethylphosphinothioyl, alkyl 2,4–dinitrophenylsulfenate, sulfate, methanesulfonate (mesylate), benzylsulfonate, and tosylate (Ts). For protecting 1,2– or 1,3–diols, the protecting groups include methylene acetal, ethylidene acetal, 1–t–butylethylidene ketal, 1–phenylethylidene ketal, (4–methoxyphenyl)ethylidene acetal, 2,2,2–trichloroethylidene acetal, acetonide, cyclopentylidene ketal, cyclohexylidene ketal, cycloheptylidene ketal, benzylidene acetal, p–methoxybenzylidene acetal, 2,4–dimethoxybenzylidene ketal, 3,4–dimethoxybenzylidene acetal, 2–nitrobenzylidene acetal, methoxymethylene acetal, ethoxymethylene acetal, dimethoxymethylene ortho ester, 1–methoxyethylidene ortho ester, 1–ethoxyethylidine ortho ester, 1,2–dimethoxyethylidene ortho ester, α–methoxybenzylidene ortho ester, 1–(N,N–dimethylamino)ethylidene derivative, α–

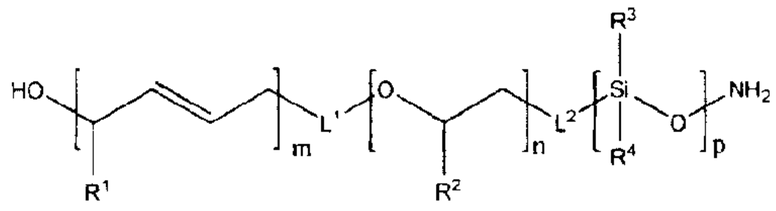
(N,N'–dimethylamino)benzylidene derivative, 2–oxacyclopentylidene ortho ester, di–t–butylsilylene group (DTBS), 1,3–(1,1,3,3–tetraisopropyldisiloxanylidene) derivative (TIPDS), tetra–t–butoxydisiloxane–1,3–diylidene derivative (TBDS), cyclic carbonates, cyclic boronates, ethyl boronate, and phenyl boronate.

[0066] One of ordinary skill in the art will appreciate that the choice of hydroxyl and amine protecting groups can be such that these groups are removed at the same time (e.g., when both protecting groups are acid labile or base labile). Alternatively, such groups can be removed in a step-wise fashion (e.g., when one protecting group is removed first by one set of removal conditions and the other protecting group is removed second by a different set of removal conditions). Such methods are readily understood by one of ordinary skill in the art.

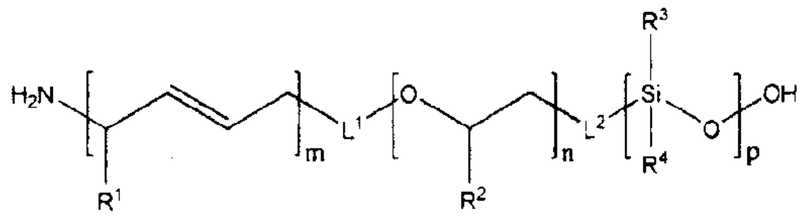
[0067] In certain embodiments, the present invention provides a compound of any of formulae **II-a**, **II-b**, **II-c**, and **II-d**:



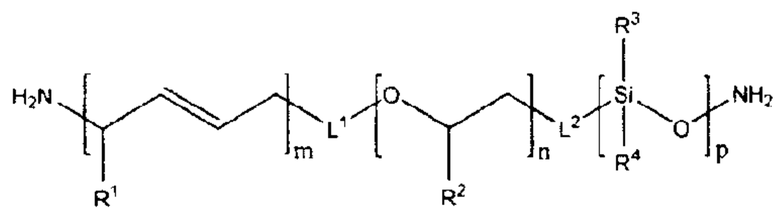
II-a



II-b



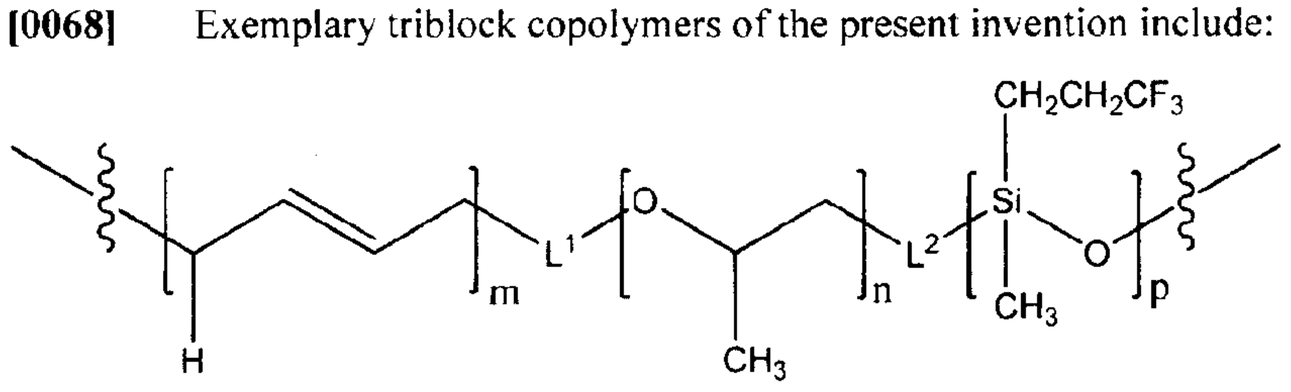
II-c



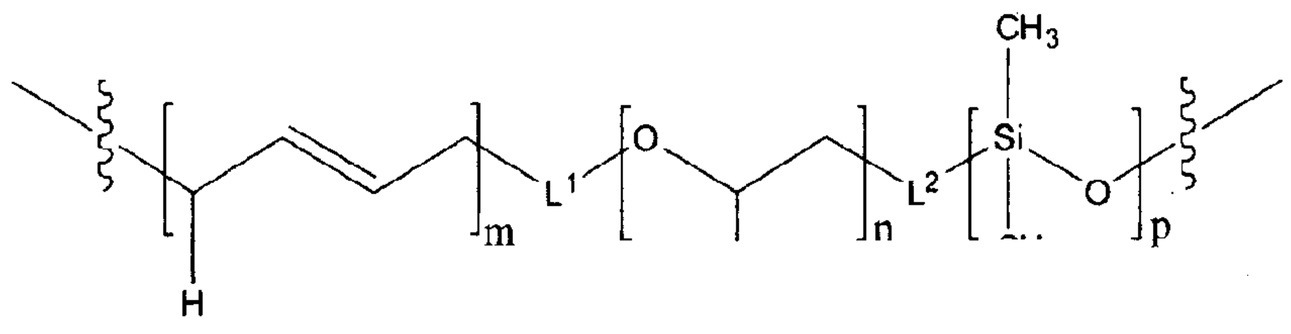
II-d

wherein each of m, n, p, L^1, L^2, R^1, R^2, R^3, and R^4 is as defined and described herein.

[0068] Exemplary triblock copolymers of the present invention include:



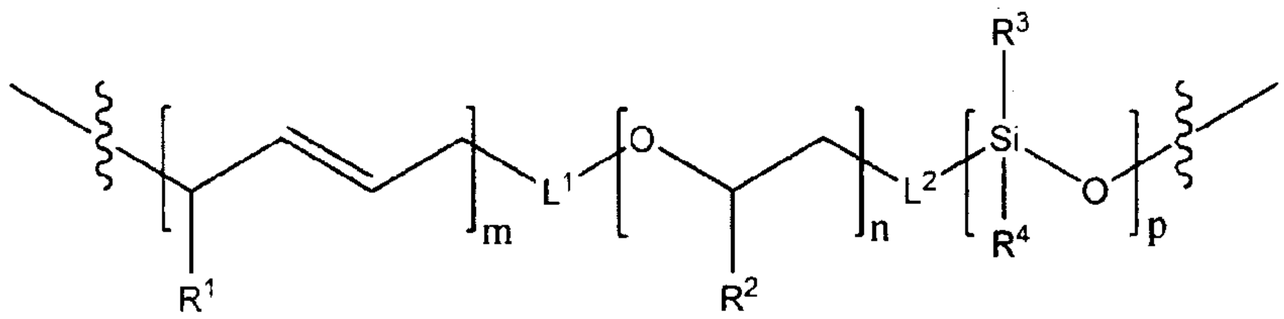
and



wherein each of L^1, L^2, m, n, and p is as defined and described herein.

[0069] In some embodiments, the present invention provides a polymer foam, comprising:

(a) one or more triblock copolymers of formula **I**:



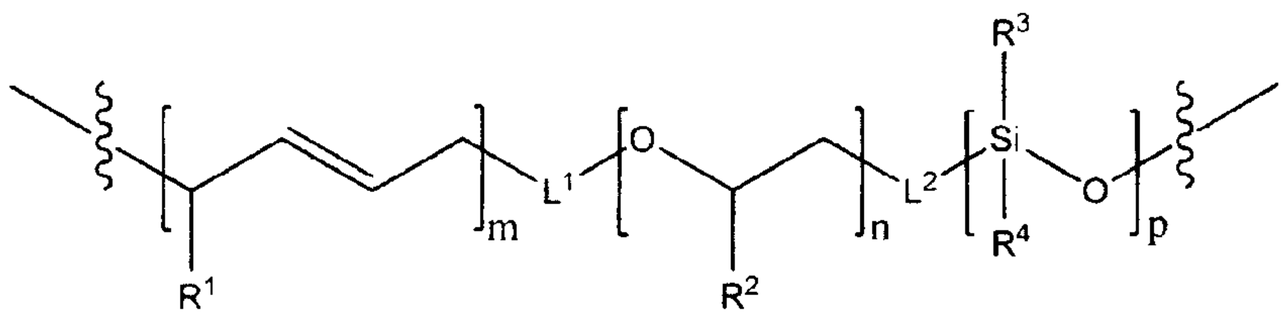
wherein each of m, n, p, L^1, L^2, R^1, R^2, R^3, and R^4 is as defined and described herein; and

(b) wherein the copolymers are chemically interspersed (bound) between urethane and/or urea linkages (i.e., at the bond designated with ξ).

[0070] The invention further provides a pre-formed soft segment of the formula **I** as defined above. In some embodiments, the present invention provides a polyurethane/urea foam comprising a soft segment triblock copolymer of formula **I**.

[0071] In some embodiments, the present invention provides a viscoelastic biostable foam, comprising:

(a) one or more triblock copolymers of formula **I**:



wherein each of m, n, p, L^1, L^2, R^1, R^2, R^3, and R^4 is as defined and described herein; and

(b) wherein the copolymers are chemically interspersed (bound) between urethane and/or urea linkages (i.e., at the bond designated with ξ).

[0072] It has been surprisingly found that polyurethanes and/or polyureas comprising a triblock copolymer of the present invention are stable to gastric fluid. Such polyurethanes and

polyureas prepared using triblock copolymers of the present invention are viscoelastic and stable to gastric fluid. In some embodiments, a provided viscoelastic material is a foam.

[0073] In certain embodiments, a provided biostable foam is stable to gastric fluid. In some embodiments, a provided biostable foam is stable to gastric fluid for at least one year. In some embodiments, a provided biostable foam is stable to gastric fluid for at least 3 months, for at least 4 months, for at least 5 months, for at least 6 months, for at least 7 months, for at least 8 months, for at least 9 months, for at least 10 months, for at least 11 months, or for at least one year. Methods for determining stability of a provided biostable foam are known in the art utilizing simulated gastric fluid and include those described in detail in the Exemplification, *infra*.

[0074] In some embodiments, a provided viscoelastic foam, comprising a triblock copolymer of the present invention, is characterized in that the foam takes up less than about 30% by weight of water at equilibrium. In certain embodiments, a provided viscoelastic foam takes up less than about 5%, less than about 10%, less than about 15%, less than about 20%, less than about 25%, or less than about 30% by weight of water at equilibrium. One of ordinary skill in the art will appreciate that such chemical stability (i.e., in gastric fluid and therefore at very low pH) and hyrophobicity (i.e., water uptake of less than about 30% by weight) are characterisitics that differ dramatically from known siloxane polymers that are utilized in, e.g., the manufacture of contact lenses. For example, siloxane polymer that are utilized in, e.g., the manufacture of contact lenses require a water uptake of 50-120%.

[0075] As described above, the present invention provides a viscoelastic foam comprising a triblock copolymer of the present invention. It was suprisingly found that a provided foam has a high elongation capacity and the ability to recover very slowly following elongation. Indeed, it was found that a provided viscoelastic foam has an elongation capacity of about 200-1200%. In some embodiments, a provided viscoelastic foam has an elongation capacity of about 500%.

[0076] In some embodiments, a provided viscoelastic foam has a tensile strength of about 0.1 to about 1.0 MPa. In certain embodiments, a provided viscoelastic foam has a tensile strength of about 0.25 to about 0.5 MPa.

[0077] In some embodiments, a provided viscoelastic foam has a Young's Modulus of about 0.05 to about 1.0 MPa. In certain embodiments, a provided viscoelastic foam has a Young's Modulus of about 0.05 to about 0.5 MPa.

[0078] One of ordinary skill in the art will appreciate that, depending upon the physical characteristics required for a particular use of a provided foam, a foam of varying densities can be prepared. For example, a valve having a thinner wall would require a foam having a higher density than a similar valve having a thicker wall in order to result in each valve having a similar physical characteristic (e.g., tensile strength, and the like). Thus, in certain embodiments, a provided viscoelastic foam has a density of 0.1 to 1.5 g/cm^3. In certain embodiments, a provided viscoelastic foam has a density of 0.3 to 1.2 g/cm^3. In certain embodiments, a provided viscoelastic foam has a density of 0.8 to 0.9 g/cm^3. In some embodiments, a provided viscoelastic foam has a density of 0.5 to 0.6 g/cm^3.

EXEMPLIFICATION

Example 1 - Synthesis of a hydroxyl terminated, triblock copolymer based on polybutadiene, polyalkylether and poly(trifluoromethyl siloxane)

[0079] Step 1 – synthesis of a fluorosiloxane based triblock copolymer pre-soft-segment:

[0080] This is a 2 stage process. In the first stage silanol terminated poly(trifluoropropyl methyl siloxane) is converted into its dihydride derivative. In the next stage, this dihydride derivative is reacted with the allyl terminated poly(propylene glycol).

[0081] The synthetic procedure is as follows:

[0082] Stage 1:

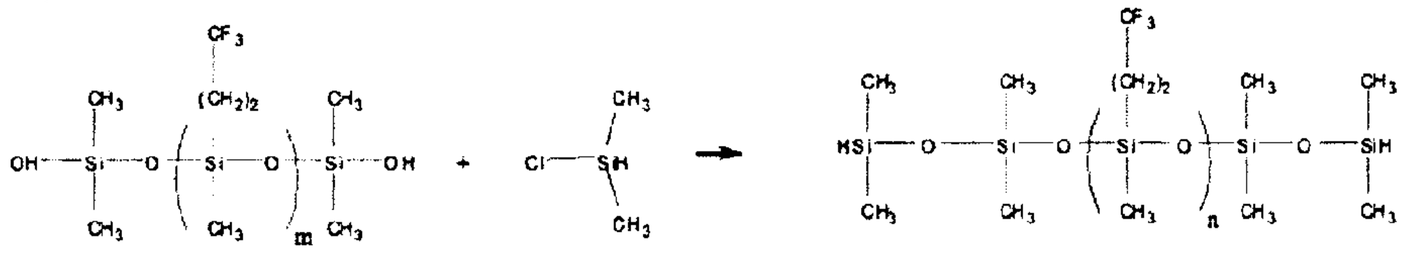
[0083] To a 4 neck separable flask fitted with mechanical stirrer, was added 40 g of Silanol terminated poly(trifluoropropyl methylsiloxane) (FMS-9922 from Gelest Inc.) and this was mixed with 50ml of toluene and fitted with a continuous flush of Nitrogen. To the reaction mixture 7.57 g of dimethyl chlorosilane (DMCS, from Sigma Aldrich) was added slowly over about 20 minutes keeping the temperature of the mixture constant at 30°C. With each addition of dimethyl chlorosilane, the mixture became hazy but cleared in a short period of time. Once the addition of dimethyl chlorosilane was complete, the mixture was heated to 90 °C for 3 hours. The reaction was then washed with excess water several times to reduce the acidity of the mixture. The resulting mixture was dried over silica gel, filtered and vacuumed to remove solvent and traces of water at 65 °C overnight. A clear fluid was then obtained with a very

strong Si-H band in infra red spectroscopy (IR) at 2130 cm^{-1} , which confirms the reaction. GPC analysis showed the molecular weight to be 1200 g/mol.

[0084] Stage 2:

[0085] To 90 ml of reagent grade toluene in a 4 neck separable flask fitted with mechanical stirrer, 46.67g of allyl terminated poly(propylene glycol) (MW=700g/mol, Jiangsu GPRO Group Co.) was added and then heated to reflux. Then 40 g of hydride terminated FMS-9922 was dissolved in 50 mL of reagent grade toluene and the temperature raised to around 90°C. To the reaction mixture 2 drops of hexachloroplatinic (IV) acid (0.01 M H_2PtCl_6 from Sigma) solution in isopropanol (by Merck) was then added. After this catalyst solution had been added, the mixture was refluxed for 1 hour and the solvent distilled off in order to get the final product. The reaction was followed by H-NMR and gel permeation chromatography (GPC) confirmed the final molecular weight to be 2700 g/mol.

Step 1



Step 2

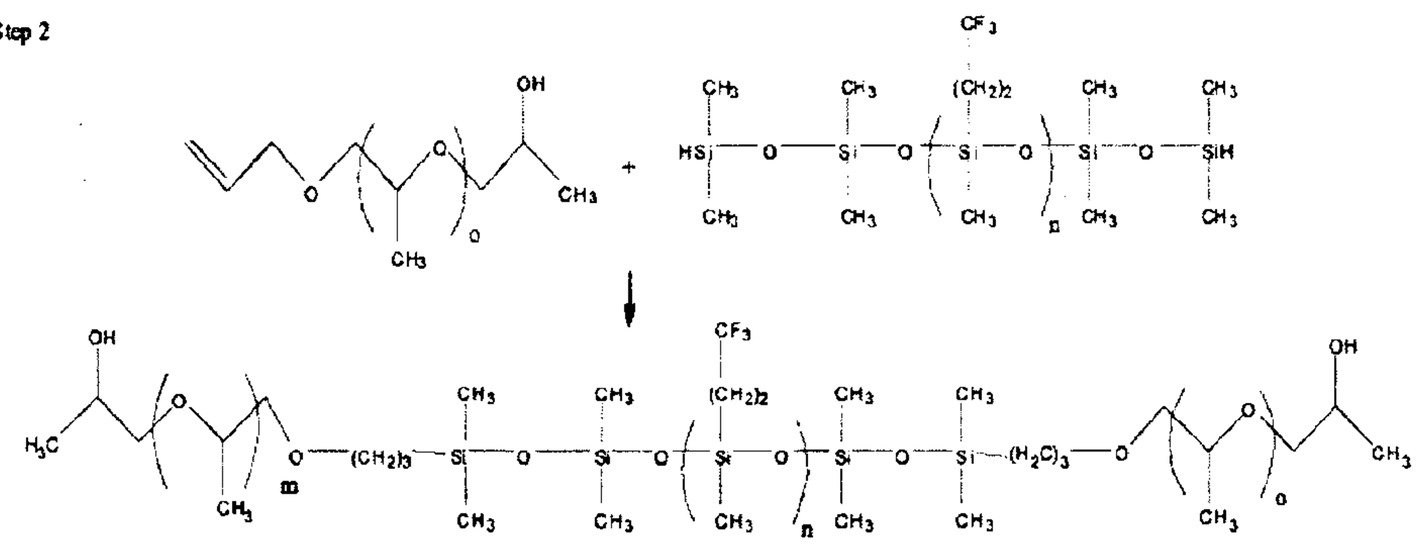


Table 1. Resulting polymer block ratios

Stoiciometric ratios for reaction product:

Polymer block	PO	F-SiO	PO
	m	n	o

Ratio	11	9.7	11

Example 2 - Preparation of polyurethane foam from the triblock copolymer of example 1:

[0086] The process for preparing the foam was a two-step procedure:

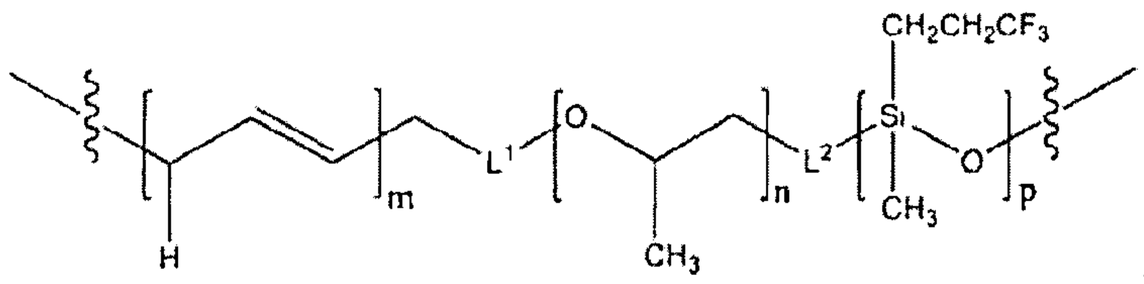
[0087] Step 1) First, a mixture was made with 0.041 g of DABCO LV-33 (Airproducts), 0.10 g of Zinc neodecanoate (Bicat Zn from Shepherd chemicals), 0.467g of diethanol amine (DEOA, from Sigma), 5.0 g of synthesized block copolymer from Example 1, 0.250 g water and 0.05 g of surfactant (Silsurf C-208 from Siltech Corp.) in a plastic flat bottomed container. This is then thoroughly mixed for 30 sec until a homogenous mixture was obtained.

[0088] Step 2) To the above mixture, 15 g of a methylene diphenyl isocyanate (MDI) based polybutadiene pre-polymer (Krasol NN3a from Sartomer) was added. This was then thoroughly mixed by a mechanical stirrer for about 30 seconds. The material was then molded and cured at 70 °C for 2.5 hours and post cured at 50 °C for another 3 hours.

Example 3 - Preparation of a thermoplastic polyurethane from the triblock copolymer of example 1:

[0089] To 30g of a methylene diphenyl isocyanate (MDI) based polybutadiene pre-polymer (Krasol NN3a from Sartomer) was added 50 g of THF. This was mixed for about 5 min to dissolve the pre-polymer and was then transferred to a four neck separable flask. To this was added 0.2 g of zinc neodecanoate (BiCat Zn from Shepherd Chemicals) and 9.5 g of the triblock copolymer synthesized as described above in Example 1. A mechanical agitator was attached and the reactor was fitted with a nitrogen purge. The mixture was stirred for 24 h and the THF was then removed under vacuum. The resulting viscous polymer was then poured into a Teflon® dish and the remaining solvent was removed under vacuum for 24 h at 50 °C.

[0090] The final product has the formula:



Example 4 – Synthesis of a triblock copolymer based on polybutadiene, polyalkylether and poly(dimethyl siloxane)

[0091] Step 1 – Synthesis of a dimethylsiloxane based triblock copolymer pre-soft-segment:

[0092] To 130 mL of reagent grade toluene in a separable flask fitted with a mechanical stirrer, was added 64 g of allyl terminated poly(propylene glycol) (MW=700g/mol, Jiangsu GPRO Co.) and both were mixed and heated to reflux. Then 40 g of hydride terminated poly(dimethyl siloxane) (Silmer H Di 10 by Siltech Corp.) was dissolved in 50 mL reagent grade toluene and the temperature raised to around 90 °C. To this reaction mixture 2 drops of hexachloroplatinic (IV) acid (0.01M H_2PtCl_6 from Sigma) solution in isopropanol was added. After this catalyst solution was added, the mixture was refluxed for 1 hour and then the solvent was distilled off in order to get the final product. The reaction was followed with H-NMR and gel permeation chromatography (GPC) confirmed the final molecular weight of the product to be 2300g/mol.

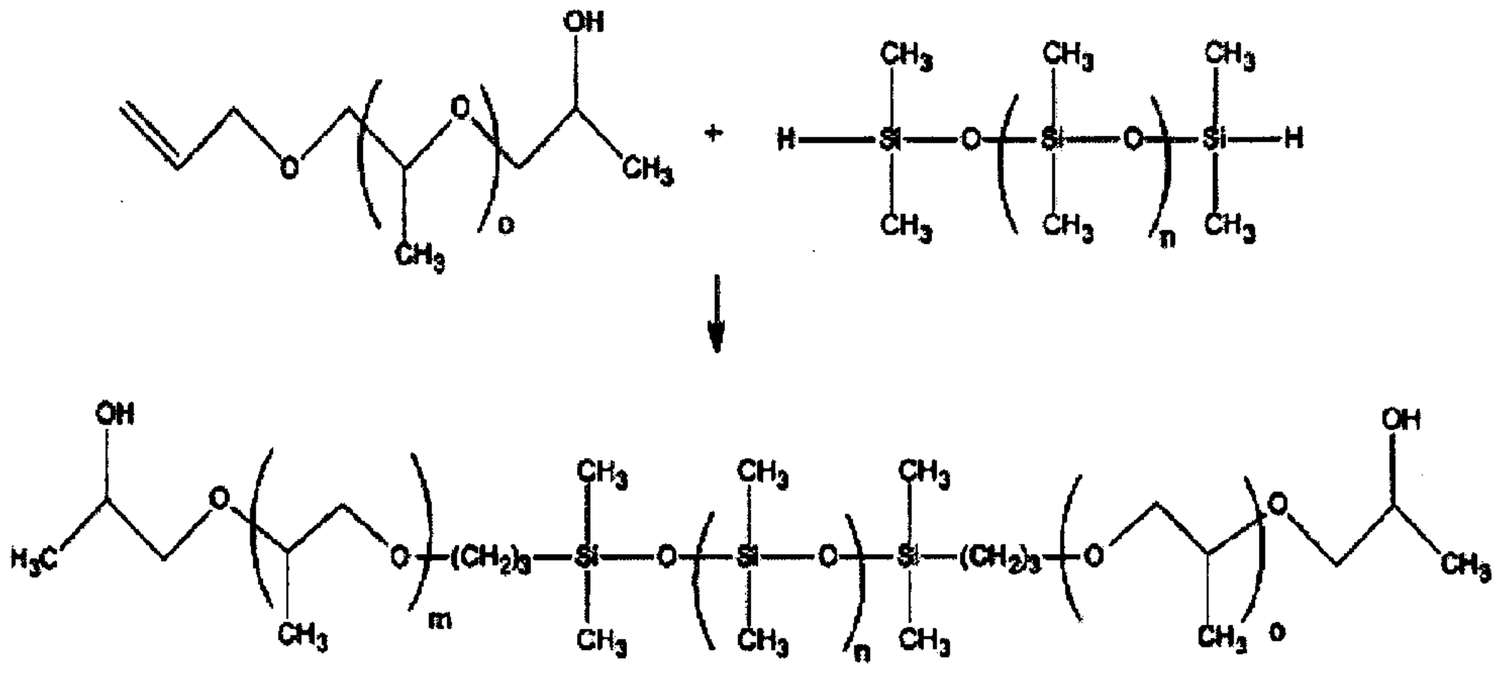


Table 2. Polymer block ratios

Stoiciometric ratios for reaction product:

Polymer block	PO	SiO	PO
	m	n	o
Ratio	11	11	11

Example 5 Preparation of a crosslinked water blown foam from the triblock copolymer of example 4:

[0093] The process for preparing the foam was a two-step procedure:

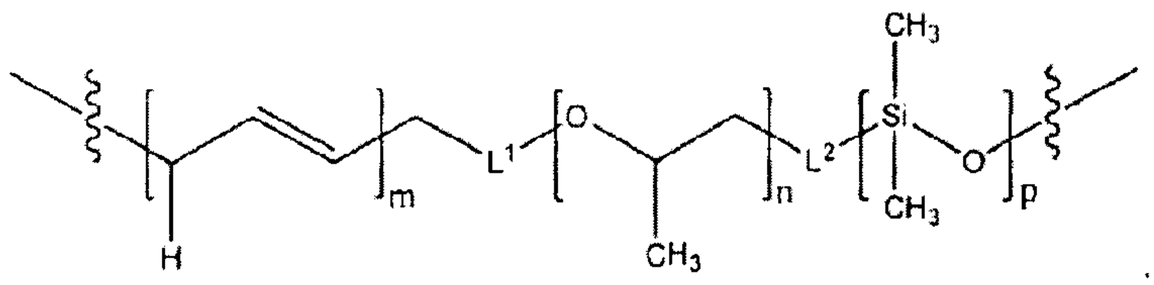
[0094] Step 1) First, a mixture was made with 0.041 g of DABCO LV-33 (Airproducts), 0.10 g of zinc neodecanoate (Bicat Zn from Shepherd chemicals), 0.467 g of diethanolamine (DEOA, from Sigma), 5.0 g of triblock copolymer synthesised as described above in example 4, 0.250 g water and 0.05 g of surfactant (Silsurf® C-208 from Siltech Corp.) in a plastic flat bottomed container. This is then thoroughly mixed for 30 sec until a homogenous mixture was obtained.

[0095] Step 2) To the above mixture, 15 g of a methylene diphenyl isocyanate (MDI) based polybutadiene pre-polymer (Krasol® NN3a from Sartomer) was added. This was then thoroughly mixed by a mechanical stirrer for about 30 seconds. The material was then molded and cured at 70 °C for 2.5 h and post cured at 50 °C for another 3 h.

Example 6 - Preparation of a thermoplastic polyurethane from the triblock copolymer of example 4

[0096] To 30 g of a methylene diphenyl isocyanate (MDI) based polybutadiene pre-polymer (Krasol NN3a from Sartomer) was added 50 g of THF. This was mixed for about 5 min to dissolve the pre-polymer and was then transferred to a four neck separable flask. To this was added 0.2g of zinc neodecanoate (BiCat Zn from Shepherd Chemicals) and 9.5 g of the triblock copolymer synthesised as described above in example 4. A mechanical agitator was attached and the reactor was fitted with a nitrogen purge. The mixture was stirred for 24 h and the THF was then removed under vacuum. The resulting viscous polymer was then poured into a Teflon dish and the remaining solvent was removed under vacuum for 24 h at 50 °C.

[0097] The final product has the formula:



Example 7 – Use

[0098] Devices for use in the gastrointestinal system have historically not been made from specifically designed materials. Off the shelf materials used for application in the corrosive environment of the stomach have limited biostability and generally lose their functionality after a short time.

[0099] In certain embodiments, the foam of the invention can be used for production of a valve of the type described in our US 2007/0198048,

In certain embodiments, the foam of the invention can be used for production of a valve of the type described in our US 2010/0137998,

. The valve has an open position and a closed position. The valve will have a proximal end and a distal end. The valve material can open from the proximal direction when the action of swallowing (liquid or solid) stretches an oriface by between 100% and 3000% in circumference. The open orifice optionally closes non-elastically over a prolonged period of time, thus mimicing the body's natural response. The duration taken to close may be between 2 and 15 sec. The material can stretch to between 100% - 300% from the distal direction when gas, liquid or solids exceeds a pre-determined force of between 25cmH_2O and 60cmH_2O. In some embodiments, the material absorbs less than 15% of its own mass of water at equilibrium. In some embodiments, the material loses (leaches) less than 3% of it's own mass at equilibrium in water or alcohol. In some embodiments, the material loses less than 10% of its tensile strength when immersed in a simulated gastric fluid at pH 1.2 for 30 days. In some embodiments, the valve material loses less than 25% of its % elongation when immersed in a simulated gastric fluid at pH 1.2 for 30 days.

Example 8 – Use

[00100] The thermoplastic material of the invention may be applied to a medical device as a coating or additionally may be extruded into a specific shape. A solution of the thermoplastic polyurethane may be applied to a stent or other device, which is held on a PTFE mandrel. A continuous coating will be formed through the evaporation of the carrier solvent. This will in turn provide a protective coating to a stent ot other medical device.

[00101] By evaporation of the solvent used in the production of the thermoplastic polyurethane a solid polymer suitable for extrusion can be formed. For example the polymer produced in example 2 may be extruded at 190°C with 5Kg of force resulting in a Melt Flow

Index (ISO 1133) of 0.475g/10mins. Such an extrusion could be used to build a catheter or other tubular device.

Example 9 - Valve functional testing

[00102] The healthy lower esophageal sphincter (LES) remains closed until an individual induces relaxation of the muscle by swallowing and thus allowing food to pass in the antegrade direction. Additionally when an individual belches or vomits they generate enough pressure in the stomach in the retrograde direction to overcome the valve. An anti-reflux valve must enable this functionality when placed in the body, thus a simple functional test is carried out to asses performance.

[00103] It has been reported that post fundoplication patients have yield pressures between 22 – 45 mmHg and that most of the patients with gastric yield pressure above 40 mmHg experienced problems belching. *See Yield pressure, anatomy of the cardia and gastro-oesophageal reflux.* Ismail, J. Bancewicz, J. Barow British Journal of Surgery. Vol: 82, 1995, pages: 943-947. Thus, in order to facilitate belching but prevent reflux, an absolute upper GYP value of 40 mmHg (550 mmH_2O) is reasonable. It was also reported that patients with visible esophagitis all have gastric yield pressure values under 15 mmHg, therefore, there is good reason to selectively target a minimum gastric yield pressure value that exceeds 15 mmHg. *See* Id. An appropriate minimum gastric yield pressure value would be 15mmHg + 25% margin of error thus resulting in a minimum effective valve yield pressure value of 18.75 mmHg or 255 mmH_2O.

[00104] The test apparatus consists of a 1m high vertical tube to which is connected a peristaltic pump and a fitting that is designed to house the valve to be tested.

[00105] The valve to be tested is placed in a water bath at 37 °C for 30 minutes to allow its temperature to equilibrate. Once the temperature of the valve has equilibrated it is then installed into the housing such that the distal closed end of the valve faces the inside of the test apparatus. The pump is then switched on at a rate of 800 ml/min to begin filling the vertical tube. The rising column of water exerts a pressure that forces the valve shut initially. As the pressure in the column rises the valve reaches a point where it everts and allows the water to flow through. This point, known as the yield pressure, is then recorded and the test repeated four times.

Example 10 -Rationale for accelerated aging of material

Clinical Condition being simulated

[00106] The lower oesophagus of a normal patient can be exposed to the acidic contents of the stomach periodically without any adverse side effects. However, patients with gastro esophageal reflux disease experience damage to the mucosa of the lower oesophagus due to increased exposure to the gastric contents. Exposure of the lower oesophagus to acidic gastric contents is routinely measured in the clinic using dedicated pH measurement equipment. A typical procedure involves measuring pH over a 24-hour period. The levels of acid exposure in pathological reflux disease patients is summarised in Table 3 from six clinical references. *See* DeMeester TR, Johnson LF, Joseph GJ, et al. *Patterns of Gastroesophageal Reflux in Health and Disease* Ann. Surg. Oct 1976 459-469; Pandolfino JE, Richter JE, Ours T, et al. *Ambulatory Esophageal pH Monitoring Using a Wireless System* Am. J. Gastro 2003; 98:4; Mahmood Z, McMahon BP, Arfin Q, et al. *Results of endoscopic gastroplasty for gastroesophageal reflux disease: a one year prospective follow-up* Gut 2003; 52:34-9; Park PO, Kjellin T, Appeyard MN, et al. *Results of endoscopic gastroplasty suturing for treatment of GERD: a multicentre trial* Gastrointest endosc 2001; 53:AB115; Filipi CJ, Lehman GA, Rothstein RI, et al. *Transoral flexible endoscopic suturing for treatment of GERD: a multicenter trial* Gastrointest endosc 2001; 53 416-22; and Arts J, Slootmaekers S Sifrim D, et al. *Endoluminal gastroplication (Endocinch) in GERD patient's refractory to PPI therapy* Gastroenterology 2002; 122:A47.

Table 3. Summary of acid exposure in patients with reflux disease

Investigator	Number of patients	Details	% 24h <pH4
DeMeester	54	Combined refluxers	13.5
Pandolfino	41	Gerd	6.5
Mahmood	21	Gerd	11.11
Park	142	Gerd	8.5
Filipi	64	Gerd	9.6
Arts	20	Gerd	17
Average			11.035

Key Clinical Parameters

[00107] Considering that the lower oesophagus is exposed to the acidic pH exposure time for an average of 11% of the measurement period, an accelerated aging methodology can easily be conceived. Constant exposure of a test material to the gastric contents (or USP Simulated Gastric Fluid – Reference USP Pharmacopeia) would represent an almost 10-fold increase in the

rate of aging. Thus the time required to simulate one year of exposure of the lower oesophagus to the gastric contents is described by equation 1.

$$\left(\frac{11.035}{100}\right) \times 365 days = 40.28 days \qquad \textit{Equation 1}$$

Clinical Rationale

[00108] Immersion of test specimens in USP Simulated gastric fluid for 40.28 days at 37 °C will approximate one year's exposure of the lower oesophagus to acidic gastric contents in a GERD patient's scenario as illustrated by Table 4.

Simulated Exposure	Real Time
1 year	40.28 days
2 years	80.56 days
3 years	120.84 days

Table 4. Correlation of simulated and realtime gastric fluid exposure in a GERD patient.

Results of accelerated stability of a valve prepared from a viscoelastic foam of the present invention as described in example 5 are depicted in Figure 1. The valve is in this case of the type illustrated and described with reference to Figures 64 and 65 of US 2010/0137998.

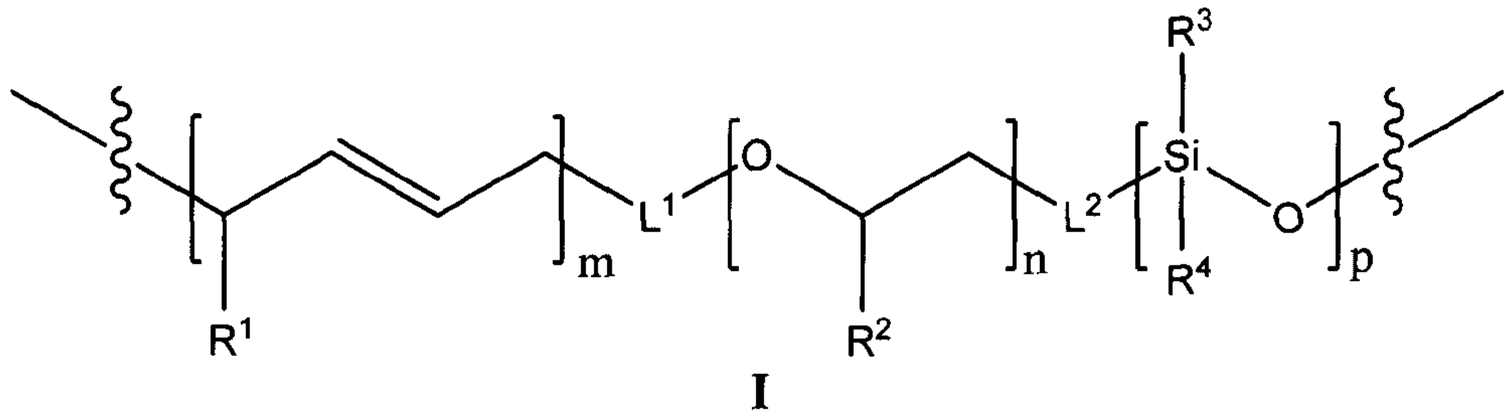
The performance of these valves was determined by measurement of the hydrostatic yield pressure or eversion pressure. The results of mass uptake testing of dogbone shaped coupons of the material described in example 5 are shown in Figure 2. Results of accelerated stability of dogbone shaped coupons prepared from a viscoelastic foam of the present invention as described in example 2 are depicted in Figure 3. The performance of these samples was determined using tensile testing.

[00109] While we have described a number of embodiments of this invention, it is apparent that our basic examples may be altered to provide other embodiments that utilize the compounds and methods of this invention. Therefore, it will be appreciated that the scope of this invention is

to be defined by the appended claims rather than by the specific embodiments that have been represented by way of example.

CLAIMS

1. A triblock copolymer of formula **I**:



I

wherein:

each $\sim$ represents a point of attachment to a urethane or urea linkage;

each of R^1, R^2, R^3, and R^4 is independently selected from one or more of halogen, R, OR, $-CO_2R$, a fluorinated hydrocarbon, a polyether, a polyester or a fluoropolymer;

each R is independently hydrogen, an optionally substituted C_{1-20} aliphatic group, or an optionally substituted group selected from phenyl, 8-10 membered bicyclic aryl, a 4-8 membered monocyclic saturated or partially unsaturated heterocyclic ring having 1-2 heteroatoms independently selected from nitrogen, oxygen, or sulphur, or 5-6 membered monocyclic or 8-10 membered bicyclic heteroaryl group having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

each of m n and p is independently 2 to 100; and

each of L^1 and L^2 is independently a bivalent C_{1-20} hydrocarbon chain wherein 1-4 methylene units of the hydrocarbon chain are optionally and independently replaced by –O-, -S-, -N(R)C(O)O-, -N(R)C(O)N(R)-, -OC(O)N(R)-, -N(R)-, -C(O)-, -C(O)N(R)-, -N(R)C(O)-, $-SO_2-$, $-SO_2N(R)-$, $-N(R)SO_2-$, -OC(O)-, –C(O)O-, or a bivalent cycloalkylene, arylene, heterocyclene, or heteroarylene.

2. The copolymer according to claim 1, wherein R^1 and R^2 are methyl, one or both of R^3 and R^4 is independently a C_{1-20} hydrocarbon chain wherein 1-4 methylene units of the hydrocarbon chain are optionally and independently substituted by halogen, and L^1 and L^2 are independently a bivalent C_{1-20} hydrocarbon chain wherein 1-4 methylene units of the hydrocarbon chain are optionally and independently replaced by –NHC(O)O- or –NHC(O)NH-.

3. The copolymer according to claim 1, wherein R^1 and R^2 are methyl, one or both of R^3 and R^4 is independently a C_{1-20} hydrocarbon chain wherein 1-4 methylene units of the hydrocarbon chain are optionally and independently substituted by halogen, L^1 is –NHC(O)O- or –NHC(O)NH-, and L^2 is a C_{1-20} hydrocarbon chain.

4. The copolymer according to claim 1, wherein R^1 and R^2 are methyl, one or both of R^3 and R^4 is independently a C_{1-20} hydrocarbon chain, L^1 is –NHC(O)O- or –NHC(O)NH-, and L^2 is a C_{1-20} hydrocarbon chain.

5. The copolymer according to claim 1, wherein m and p are each independently between 2 and 50 and n is between 2 and 20.

6. The copolymer according to claim 5, wherein m and p are each independently between 2 and 30 and n is between 2 and 20.

7. The copolymer according to claim 5, wherein each of m, n and p are 8-16.

8. The copolymer according to any one of claims 1-7, wherein one or more of R^1, R^2, R^3, and R^4 is independently an optionally substituted C1-6 alkyl.

9. The copolymer according to claim 8, wherein each of R^1, R^2, R^3 and R^4 is independently methyl, ethyl, propyl, isopropyl, cyclopropyl, butyl, isobutyl, or cyclobutyl.

10. The copolymer according to claim 1, wherein each of R^1, R^2, R^3 and R^4 is independently mono-, di-, tri, or perfluorinated methyl, ethyl, propyl, butyl, or phenyl.

11. The copolymer according to claim 8, wherein each of R^1, R^2, R^3 and R^4 is independently methyl, ethyl, propyl, trifloromethyl, trifluoroethyl, or trifluoropropyl.

12. The copolymer according to claim 1, wherein R^1 is hydrogen, methyl, chloro or fluoro.

13. The copolymer according to claim 1, wherein R^2 is hydrogen or methyl.

14. The copolymer according to claim 1, wherein R^3 is methyl, phenyl, fluoro, or $-CH_2CH_2F$.

15. The copolymer according to claim 1, wherein R^4 is methyl, phenyl, fluoro, or $-CH_2CH_2F$.

16. The copolymer according to any one of claims 1-15 wherein each of L^1 and L^2 is independently a bivalent C_{1-20} alkylene chain.

17. The copolymer according to claim 16 wherein each of L^1 and L^2 is independently a bivalent C_{1-10} alkylene chain.

18. The copolymer according to claim 17 wherein each of L^1 and L^2 is independently a bivalent methylene, ethylene, propylene, or butylene chain.

19. The copolymer according to any one of claims 1-17 wherein each of L^1 and L^2 is independently $-OCH_2-$, $-OCH_2CH_2-$, $-OCH_2CH_2CH_2-$, or $-OCH_2CH_2CH_2CH_2-$.

20. The copolymer according to any one of claims 1-15 wherein each of L^1 and L^2 is independently a bivalent C_{1-6} alkylene chain wherein at least one methylene unit of the chain is replaced by -O and at least one methylene unit of the chain is replaced by a bivalent arylene.

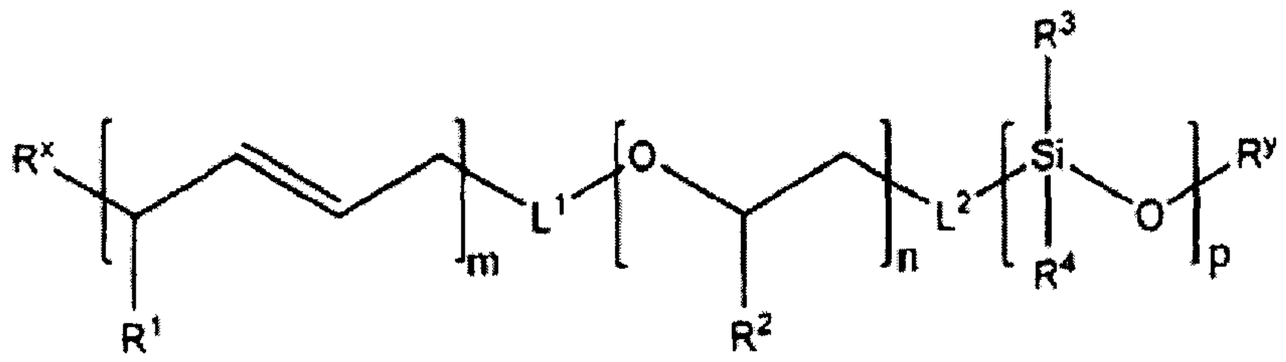
21. The copolymer according to claim 20 wherein each of L^1 and L^2 is independently $-OCH_2$-phenylene-, $-OCH_2CH_2$-phenylene-, $-OCH_2CH_2$-phenylene-CH_2-, or $-OCH_2CH_2CH_2CH_2$-phenylene-.

22. The copolymer according to claim 1, wherein at least one of L^1 and L^2 is a bivalent C_{1-20} hydrocarbon chain wherein 1-4 methylene units of the hydrocarbon chain are optionally and independently replaced by: –N(H)C(O)N(H)-, -N(H)C(O)O-, or -OC(O)N(H)-.

23. The copolymer according to claim 1, wherein L^1 is a urethane.

24. The copolymer according to claim 1, wherein L^2 is $–CH_2CH_2-$.

25. A triblock copolymer of formula II:



II

wherein:

each of R^x and R^y is independently –OH, $-NH_2$, a protected hydroxyl or a protected amine;

each of R^1, R^2, R^3, and R^4 is independently selected from one or more of halogen, R, OR, $-CO_2R$, a fluorinated hydrocarbon, a polyether, a polyester or a fluoropolymer;

each R is independently hydrogen, an optionally substituted C_{1-20} aliphatic group, or an optionally substituted group selected from phenyl, 8-10 membered bicyclic aryl, a 4-8 membered monocyclic saturated or partially unsaturated heterocyclic ring having 1-2 heteroatoms independently selected from nitrogen, oxygen, or sulphur, or 5-6 membered monocyclic or 8-10 membered bicyclic heteroaryl group having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulphur;

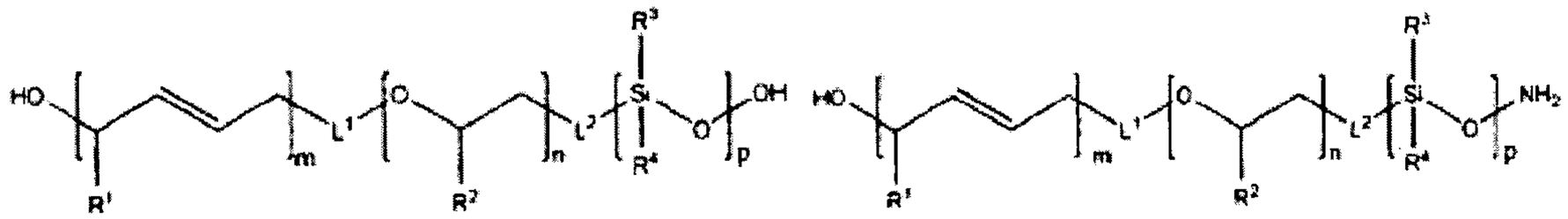
each of m, n, and p is independently 2 to 100; and

each of L^1 and L^2 is independently a bivalent C_{1-20} hydrocarbon chain wherein 1-4 methylene units of the hydrocarbon chain are optionally and independently replaced by –O-, -S-, -N(R)C(O)O-, N(R)C(O)N(R)-, -OC(O)N(R)-, -N(R)-, -C(O)-, -C(O)N(R)-, -N(R)C(O)-, $-SO_2-$,

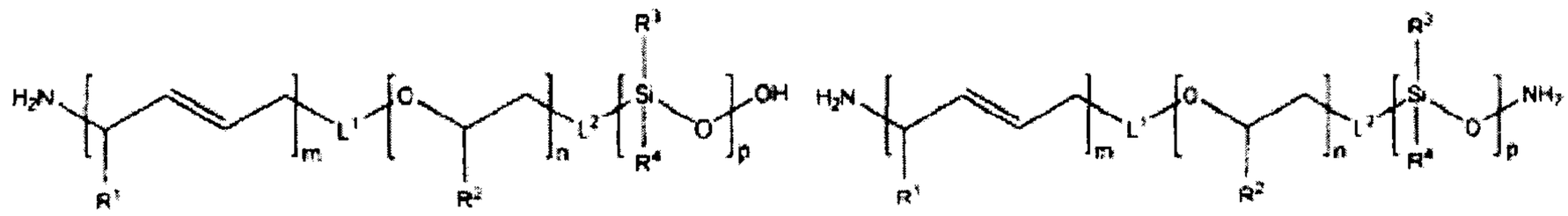
$-SO_2N(R)-$, $-N(R)SO_2-$, -OC(O)-, -C(O)O-, or a bivalent cycloalkylene, arylene, heterocyclene, or heteroarylene.

26. The copolymer according to claim 25 wherein both of R^x and R^y are –OH.

27. The copolymer according to claim 25, selected from any of formulae II-a, II-b, II-c, and II-d:



II-a



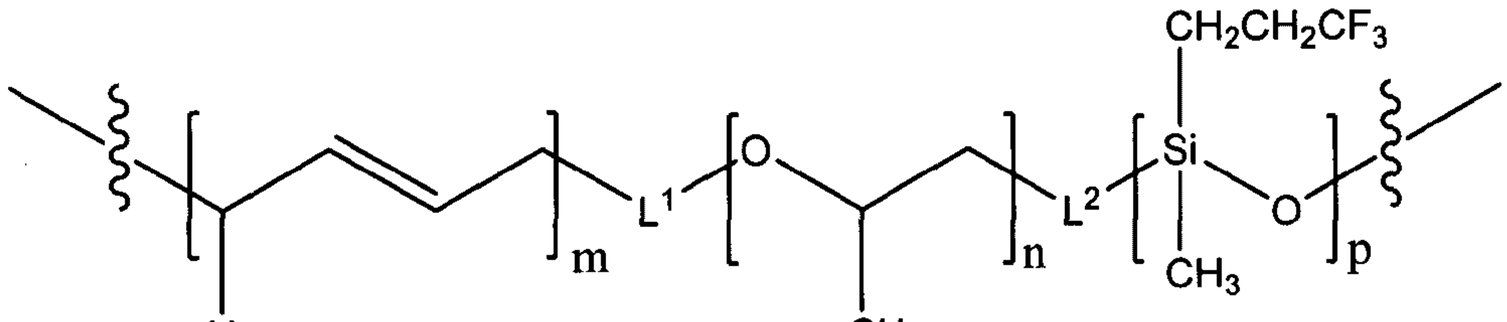
II-b

II-c

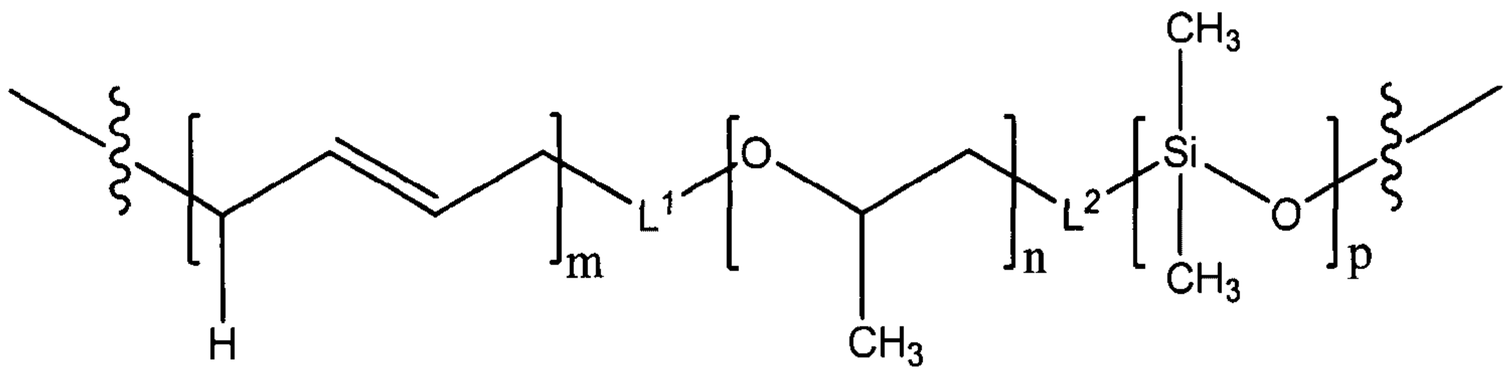
and

II-d.

28. The copolymer according to claim 1, selected from:



and



29. A biomaterial comprising the triblock copolymer according to any one of claims 1-24 or claim 28.

30. A medical device comprising the triblock copolymer according to any one of claims 1-24 or claim 28.

31. A viscoelastic biostable foam comprising the triblock copolymer according to any one of claims 1-24 or claim 28.

32. The viscoelastic biostable foam according to claim 31, comprising the triblock copolymer according to claim 28.

33. The viscoelastic biostable foam according to claim 31, wherein said foam is stable to gastric fluid for at least 3 months, for at least 4 months, for at least 5 months, for at least 6 months, for at least 7 months, for at least 8 months, for at least 9 months, for at least 10 months, for at least 11 months, or for at least one year.

34. The viscoelastic biostable foam according to claim 31, wherein said foam takes up less than 5%, less than 10%, less than 15%, less than 20%, less than 25%, or less than 30% by weight of water at equilibrium.

35. The viscoelastic biostable foam according to any one of claims 31-34, wherein said foam has an elongation capacity of 200-1200%.

36. The viscoelastic biostable foam according to any one of claims 31-35, wherein said foam has a tensile strength of about 0.1 to about 1.0 Mpa.

37. The viscoelastic biostable foam according to any one of claims 31-36, wherein said foam has a density of 0.1 to 1.5 g/cm^3.

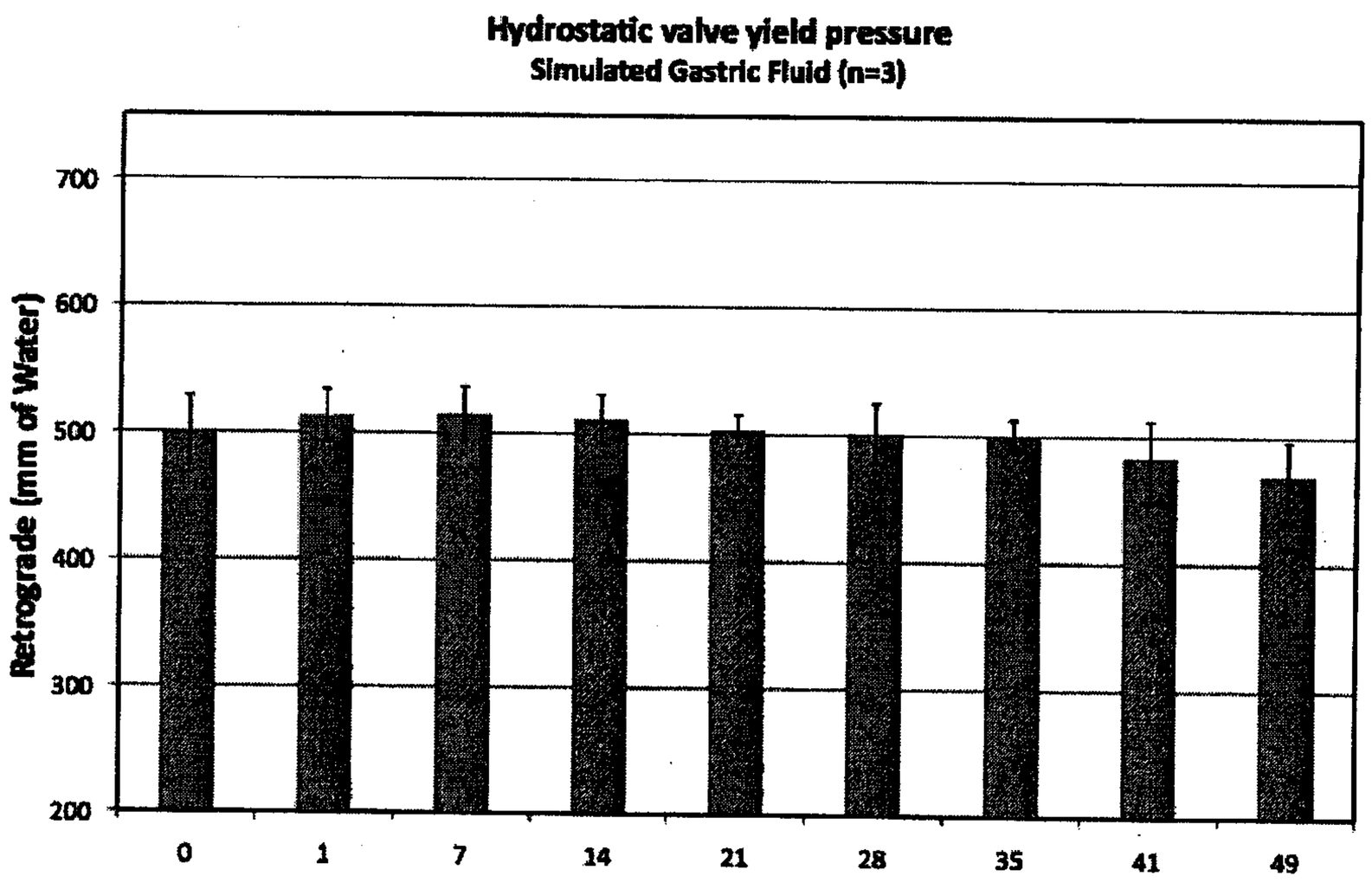

Hydrostatic valve yield pressure
Simulated Gastric Fluid (n=3)
Retrograde (mm of Water)
700
600
500
400
300
200
0
1
7
14
21
28
35
41
49
Simulated Time (month)

Figure 1

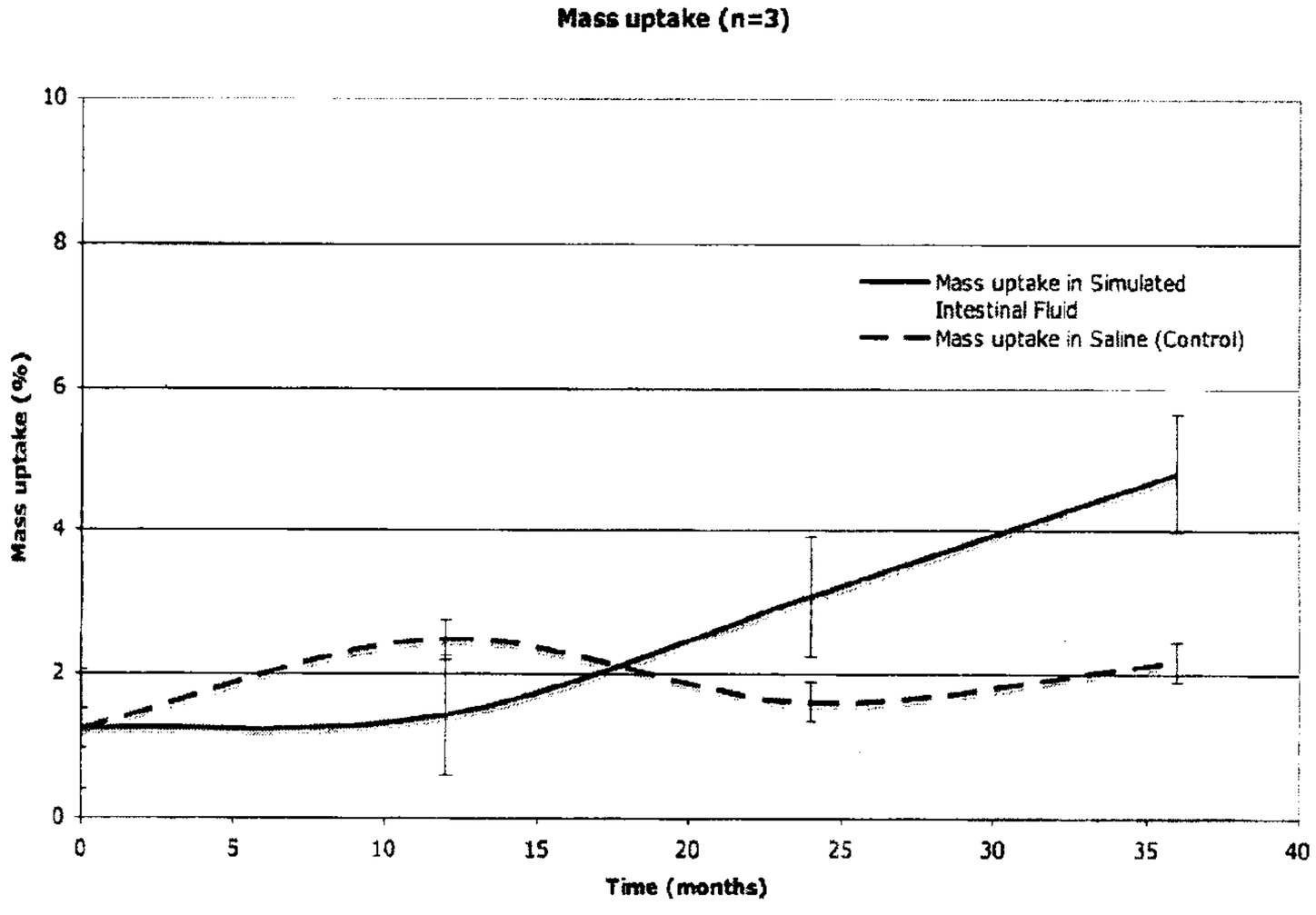

Mass uptake (n=3)
Mass uptake (%)
Time (months)
Mass uptake in Simulated Intestinal Fluid
Mass uptake in Saline (Control)
0
2
4
6
8
10
0
5
10
15
20
25
30
35
40

Figure 2

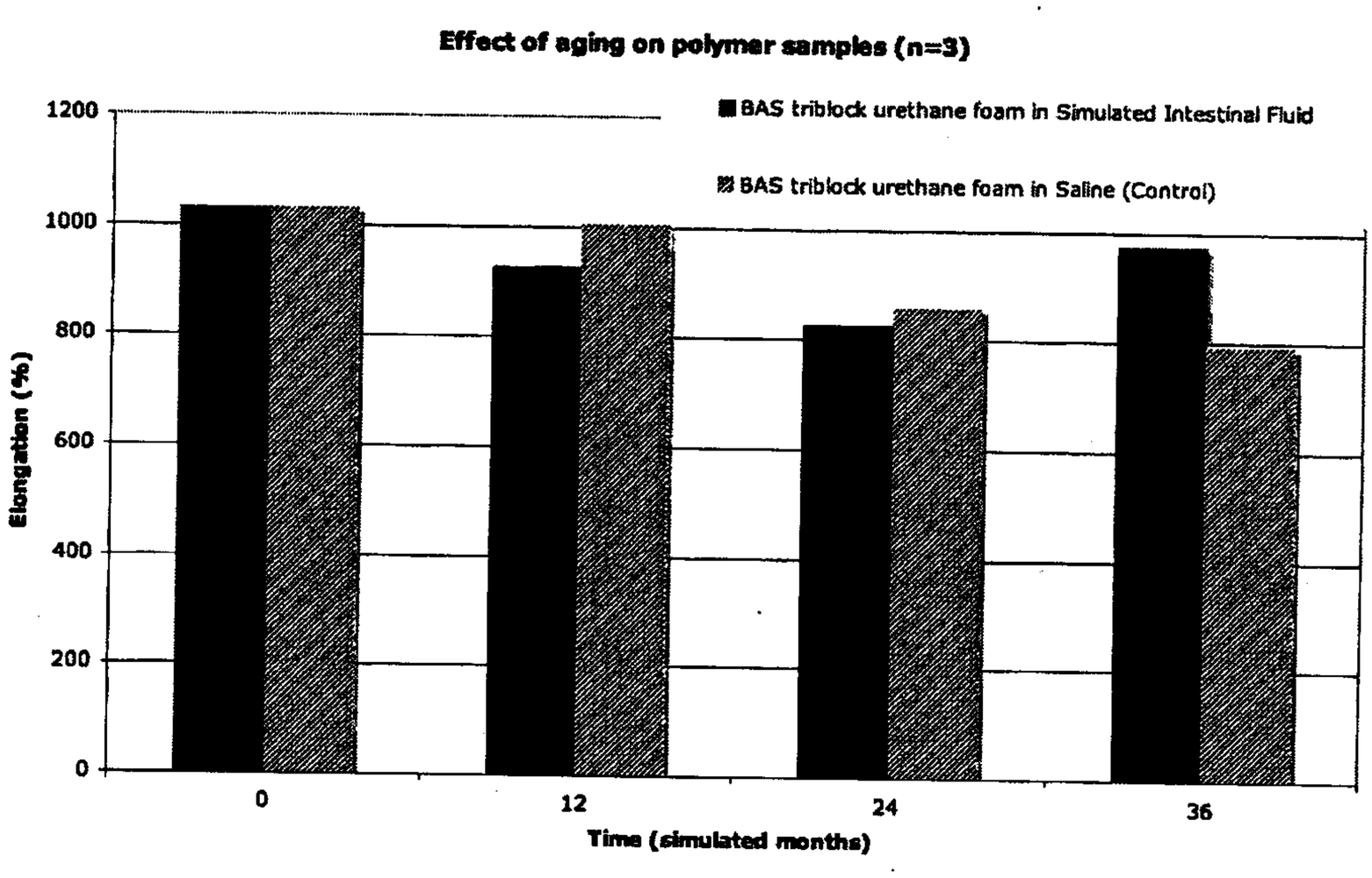
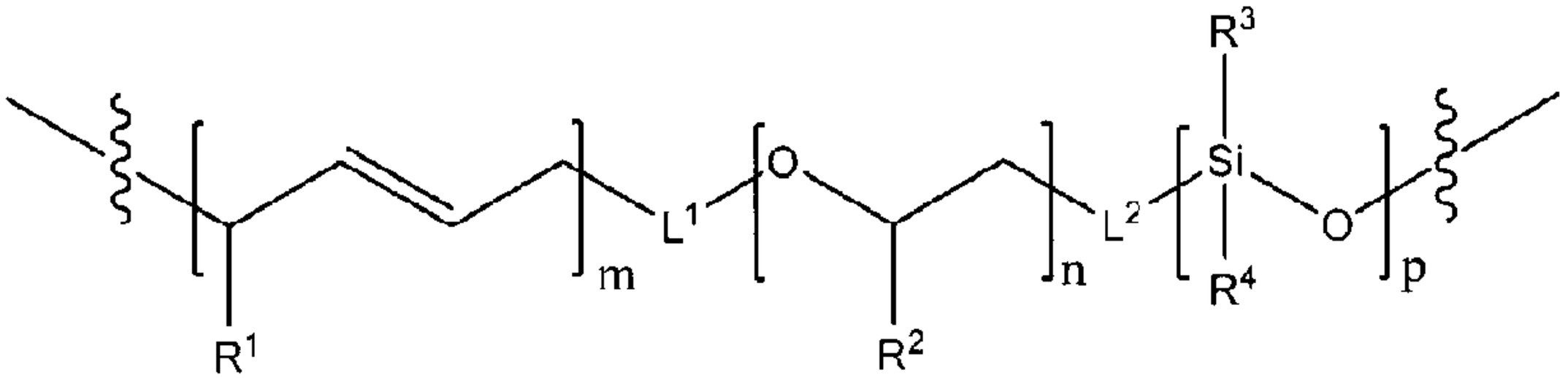

Effect of aging on polymer samples (n=3)
BAS triblock urethane foam in Simulated Intestinal Fluid
BAS triblock urethane foam in Saline (Control)
Elongation (%)
1200
1000
800
600
400
200
0
0
12
24
36
Time (simulated months)

Figure 3



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