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(54) **Title**: CONVALENTLY CROSS LINKED HYDROGELS AND METHODS OF MAKING AND USING SAME

(57) **Abstract**: A thiol-yne polymeric material and methods for producing said polymers are disclosed. The material is produced by the radically mediated polymerization of monomers having alkyne and thiol functional groups. The alkyne moiety, internal or terminal, may react with one or two thiols. Degradable monomers may be used to form degradable polymers.

COVALENTLY CROSS LINKED HYDROGELS AND METHODS OF MAKING AND USING SAME

RELATED APPLICATION

This application claims priority from U.S. Provisional Patent Application No. 61/437,435, filed on January 28, 2011 which is incorporated herein by reference in its entirety.

BACKGROUND

Materials used for tissue regeneration are designed with precise physical and biological properties. Current methods of producing materials for tissue regeneration are very costly and time consuming. This is due to specialized apparatuses and procedures to make such materials. There is a need for materials used in tissue regeneration that are low in cost, versatile and easily prepared.

SUMMARY

This disclosure provides a composition including a polymer including two or more types of monomers wherein at least a first monomer comprises at least two thiol moieties and at least a second monomer comprises at least one alkyne moiety and wherein the first and second monomers are crosslinked at bonds between the thiol and alkyne moieties. In certain embodiments the first monomer includes at least 2, 3, 4, 5, 6, 7, 8, 9 or 10 thiol moieties. In other embodiments, the second monomer includes at least 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 alkyne moieties.

In other embodiments, the first and/or second monomer is selected from poly(lactic acid) (PLA), polyglycolide (PGA), copolymers of PLA and PGA (PLGA), poly(vinyl alcohol) (PVA), poly(ethylene glycol) (PEG), poly(ethylene oxide), poly(ethylene oxide)-co-poly(propylene oxide) block copolymers (poloxamers, meroxapols), poloxamines, polyanhydrides, polyorthoesters, poly(hydroxy acids), polydioxanones, polycarbonates, polyaminocarbonates, poly(vinyl pyrrolidone), poly(ethyl oxazoline), carboxymethyl cellulose, hydroxyalkylated celluloses such as hydroxyethyl cellulose and methylhydroxypropyl cellulose, and natural polymers such as nucleic acids, polypeptides, polysaccharides or carbohydrates such as polysucrose, hyaluranic acid, dextran and similar derivatives thereof, heparan sulfate, chondroitin

sulfate, heparin, or alginate, and proteins including without limitation gelatin, collagen, albumin, or ovalbumin, or copolymers, or blends thereof. In particularly preferred embodiments, the monomers can be selected from poly(lactic acid) (PLA), poly(vinyl alcohol) (PVA), and poly(ethylene glycol) (PEG). In some embodiments, the monomers are derivatized to include a thiol or alkyne moiety. In one embodiment, one of the monomer is a four arm PEG wherein each PEG arm is chemically modified to include an alkyne at the end of the arm.

In other embodiments, the composition includes a hydrogel. The hydrogel can include more than 50% solvent by weight. In a preferred embodiment, the solvent is water and the hydrogel includes between 50 and 95% water by weight.

In another embodiments, the first or second monomers are degradable. The degradable monomer can be hydrolytically, chemically or enzymatically degradable. In certain embodiments, the first monomer comprises a peptide. Optionally, the peptide can be enzymatically degradable. This enzyme can be a protease. The peptide can be selected from adhesion peptides (such as RGD adhesion sequence), growth factors, hormones, antihormones, signaling compounds, enzymes, serum proteins, albumins, macroglobulins, globulins, agglutinins, lectins, extracellular matrix proteins, antibodies, and antigens.

In certain embodiments, the composition described herein can further include an agent that has a biological function or activity, including pharmaceutically active agents. Peptide agents can be selected from adhesion peptides (such as RGD adhesion sequence), growth factors, hormones, antihormones, signaling compounds, enzymes, serum proteins, albumins, macroglobulins, globulins, agglutinins, lectins, extracellular matrix proteins, antibodies, and antigens. Non-peptide agents that can be incorporated into the polymeric material include analgesics, antipyretics, nonsteriodal antiinflammatory drugs, antiallergics, antibacterial drugs, antianemia drugs, cytotoxic drugs, antihypertensive drugs, dermatological drugs, psychotherapeutic drugs, vitamins, minerals, anorexiants, dietetics, antiadiposity drugs, carbohydrate metabolism drugs, protein metabolism drugs, thyroid drugs, antithyroid drugs, and coenzymes. In certain embodiments, the composition described herein can further include an agricultural chemical. The agricultural chemical can be selected from fungicides, herbicides, fertilizers, pesticides, carbohydrates, nucleic acids, organic molecules, and inorganic biologically active molecules.

With respect to the above two paragraphs, it is not necessary that these agents be covalently attached to the polymer. However, in certain embodiments, these agents may be covalently attached to polymer using the same thiol-yne chemistry. In other embodiments, these agents may be covalently attached using other chemistries.

This disclosure further provides a method for producing the compositions described above including providing the first and second monomers; mixing the first and second monomers with a photoinitiator in solvent; and exposing the first and second monomers and photoinitiator to light. In certain embodiments, the photoinitiator is selected from Irgacure 2959, 184 and 651.

In one embodiment, the light is ultraviolet light. The ultraviolet light can have a wavelength between 300 and 400 nm. In other embodiments, the light can be in the visible or IR spectrum. The exposure to light can last for less than one, two, five or 20 minutes.

In other embodiments, the solvent is present at greater than 50% of the mixture of the first and second monomer, photoinitiator and solvent.

This disclosure further provides a method of culturing cells comprising growing the cells on the compositions described above. In certain embodiments, the cells are mammalian cells. The mammalian cells can be human cells. In other embodiments, the cells are primary cells or stem cells.

The disclosure further provides kits. These kits can include the compositions including two or more types of monomers wherein at least a first monomer comprises at least two thiol moieties and at least a second monomer comprises at least one alkyne moiety and wherein the first and second monomers are crosslinked at bonds between the thiol and alkyne moieties. These kits can also include the monomers and photoinitiator used to produce the compositions described herein. These kits can also include the compositions described herein as well as cells that can be cultured on these compositions as described above.

BRIEF DESCRIPTION OF THE DRAWING

Figure 1 is a line graph showing shear elastic modulus versus time.

DETAILED DESCRIPTION

The present disclosure provides a novel class of scaffolds which are thiol-yne hydrogels. These scaffolds are produced by the radical mediated polymerization of monomers containing alkyne and thiol functional groups. In certain embodiments, the scaffold is a three dimensional polymer matrix.

Thiol-yne polymerizations are radical mediated processes that take place between thiols and alkyne-containing moieties via a sequential propagation/chain-transfer process. In certain embodiments, polymerizations occur between two types of monomer. The first type of monomer is derivatized with thiol groups and the second type of monomer is derivatized with alkyne groups. The thiol monomer can be derivatized with 2, 3, 4, 5, 6, 7, 8, 9, 10 or more thiol groups. The alkyne monomer can be derivatized with 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 or more alkyne groups. For example, in this embodiment, the thiol monomer could have three thiol moieties and the alkyne monomer could have two alkyne moieties. In other embodiments, each thiol-containing component has an average of at least two thiol groups. In this embodiment, because each alkyne functional group is capable of undergoing up to two reactions with thiols, each alkyne -containing component has at least one alkyne functional group, (i.e. the monomer contains one or more triple bonds). Crosslinked gels can be readily formed by increasing the monomer functionality of one or both of the monomers to allow for more than two reactions per monomer.

In one embodiment, these scaffolds may be built upon degradable materials, such as peptides, proteins, and poly(lactic acid) blocks. In another embodiment, they can incorporate chemicals and live cells within the polymer matrix.

In one embodiment, an initiating system is used to generate radicals that initiate polymerization. Radicals may be generated by redox, thermal, enzymatic or photochemical mechanisms.

In one embodiment the initiator is a photoinitiator present in the monomer solution at a concentration of less than 5% by weight and is capable of initiating polymerization upon exposure to UV,visible or infra-Red light at an intensity general ranging from 0.1 to 200 mW/cm^2 with both higher and lower light intensities possible.

In a preferred embodiment initiator concentration and light intensity will be sufficient for polymerization to occur, resulting in a crosslinked material, often in less than 20 minutes, preferably polymerization will occur in less than 5 minutes, preferably

polymerization will occur in less than 2 minutes, more preferably polymerization will occur in less than 1 minute. Initiators include, but are not limited to Irgacure 2959, 184 and 651.

In an embodiment the initiator will be capable of initiating polymerization in a dilute monomer solution containing more than 50% solvent. Preferably the initiator is a photoinitiator capable of initiating polymerization in the presence of water, and water is preferably used as the solvent. More preferably the photoinitiator will be present in the monomer solution in an amount less than or equal to 0.5%, 1% or 5% by weight and is a water soluble photoinitiator such as but not limited to Irgacure-2959 or water soluble acyl-phosphinate initiator such as but not limited to salts of phenyl-2,4,6-trimethylbenzoylphosphinate.

As mentioned above, the resulting polymer may be crosslinked wherein at least one of the co-monomers can form more than two bonds on average. In specific embodiments, at least one of the monomers contains more than one alkyne functionality or more than two thiol functionalities. Example 4 below demonstrates the ability of the alkyne to react twice with independent thiol functional groups to produce a crosslinked polymer. In one embodiment, the thiol containing monomer contains two thiol groups and the alkyne containing monomer contains 2, 3, 4, 5, 6, 7, 8, 9 or 10 alkyne groups. In another embodiment, the alkyne containing monomer contains 1 alkyne group and the thiol containing monomer contains 3, 4, 5, 6, 7, 8, 9 or 10 thiol groups. In another embodiment, the alkyne containing monomer contains 2 alkyne groups and the thiol containing monomer contains 3, 4 or 8 yne groups. Based on this disclosure, other combinations will be understood by one skilled in the art.

In some embodiments, the monomer is derivatized to include a thiol or alkyne moiety. In preferred embodiments, the core of the monomer structure, to which the reactive yne or thiol moieties are attached, can be selected from one or more of the following: poly(lactic acid) (PLA), polyglycolide (PGA), copolymers of PLA and PGA (PLGA), poly(vinyl alcohol) (PVA), poly(ethylene glycol) (PEG), poly(ethylene oxide), poly(ethylene oxide)-co-poly(propylene oxide) block copolymers (poloxamers, meroxapols), poloxamines, polyanhydrides, polyorthoesters, poly(hydroxy acids), polydioxanones, polycarbonates, polyaminocarbonates, poly(vinyl pyrrolidone), poly(ethyl oxazoline), carboxymethyl cellulose, hydroxyalkylated celluloses such as hydroxyethyl cellulose and methylhydroxypropyl cellulose, and natural polymers such

as nucleic acids, polypeptides, polysaccharides or carbohydrates such as polysucrose, hyaluranic acid, dextran and similar derivatives thereof, heparan sulfate, chondroitin sulfate, heparin, or alginate, and proteins including without limitation gelatin, collagen, albumin, or ovalbumin, or copolymers, or blends thereof. In particularly preferred embodiments, the monomers can be selected from poly(lactic acid) (PLA), poly(vinyl alcohol) (PVA), and poly(ethylene glycol) (PEG). PLA monomers provide degradability to the system while PVA and PEG enhance the hydrophilic nature of the hydrogel and provide for the possibility of further derivatization and/or extensive crosslinking. Peptides can also be derivatized with thiol or alkyne groups.

According to the compositions and methods described herein, peptides can be monomers making up the scaffold. These monomers are derivatized with alkyne or thiol groups. Preferably, thiols are included within the peptides through the use of cysteine residues. Peptides can also be covalently attached to the scaffold matrix, but not be either the first or second monomer. In certain embodiments, these peptides can have a biological activity or function. Peptides can also be encapsulated within the matrix but not covalently attached to the matrix, In certain embodiments, these peptides can also have a biological activity or function.

Similarly, other non-peptide agents that have a biological activity or function can also be covalently attached to the scaffold matrix, but not be either the first or second monomer. This attachment can employ the same thol-yne chemistry as is used in the first or second monomer, or could use a different attachment chemistry. Non-peptide agents can also be encapsulated within the matrix but not covalently attached to the matrix,

The resulting polymers may be low density materials, and may be polymerized in the presence of solvent such as but not limited to water. In the case of hydrogels, the resultant hydrogels may contain >95%, >90%, >80%, >70%, >60% or greater than 50% solvent by weight. In some embodiments the solvent might be a mixture of two or more solvents. For certain biomedical applications it may be most desirable for the initial monomer solution to contain 50 – 95 % water by weight.

In some cases, the monomer choice is dependent on the solvent. In other embodiments, the resulting polymers can be swellable in a solvent by selecting co-monomers of a particular chemical nature. For example, In selecting monomers to form a thiol-yne hydrogel in an aqueous environment, it may be desirable to select monomers

that will that have a hydrophilic core, such as PEG, PVA, or peptides that incorporate hydrophilic residues. Gels that are compatible with other solvents can be formed using monomers that are compatible with that solvent. As one skilled in the art will recognize, such monomers can be selected from the above mentioned monomers.

In other embodiments, monomers may contain non-hydrophilic elements (other peptides, PLA segments, etc) such that they add functionality and capabilities. PLA segments, attached to a hydrophilic core, for example, will enable the hydrogel to simultaneously swell in the presence of water while being hydrolytically degradable. Peptide sequences can be incorporated for cell signaling, drug delivery, and to impart enzymatic degradability to the hydrogel.

In other embodiments, other vinyl functional monomers (enes, acrylates and methacrylates as examples) may also be included in the polymerizing mixture. For example, (meth) acrylate components, typically incorporated between 10 and 90% of the reacting monomer mixture, can be copolymerized with the thiol and yne monomers to facilitate polymer network structural differences and to change the material properties such as crosslink density, swelling and degradation.

As mentioned above, in some embodiments, degradable monomers may be incorporated in order to form a polymer that is degradable. In one embodiment, the monomers are chemically (for example under acidic or basic conditions) or hydrolytically degradable. For biological applications, it may be desirable to employ enzymatically degradable monomers. For example, monomers can consist of peptides that are cleaved by proteases such as matrix metallo proteases, serine proteases, aspartic acid proteases, threonine proteases, glutamic acid proteases and cysteine proteases. Other biological polymers that may be degraded by other enzymes may also be used.

A wide variety of molecules can be incorporated into the polymeric material through --OH groups or --SH groups including, but not limited to, peptides, proteins, agents that provide a biological activity or function (including pharmacologically active agents), and agricultural chemicals. Alternatively, such molecules can be encapsulated in the polymeric material or reacted to the polymeric material after polymerization in the event such molecules would lose functionality if chemically bound to the polymeric material or if present during the polymerization, respectively. For example, types of proteins that can be incorporated into the polymeric material include adhesion peptides (such as RGD adhesion sequence), growth factors, hormones, antihormones, signaling

compounds, enzymes, serum proteins, albumins, macroglobulins, globulins, agglutinins, lectins, extracellular matrix proteins, antibodies, and antigens. Types of pharmacologically active agents that can be incorporated into the polymeric material include analgesics, antipyretics, nonsteriodal antiinflammatory drugs, antiallergics, antibacterial drugs, antianemia drugs, cytotoxic drugs, antihypertensive drugs, dermatological drugs, psychotherapeutic drugs, vitamins, minerals, anorexiants, dietetics, antiadiposity drugs, carbohydrate metabolism drugs, protein metabolism drugs, thyroid drugs, antithyroid drugs, and coenzymes. Types of agricultural chemicals that can be incorporated into the polymeric material include fungicides, herbicides, fertilizers, pesticides, carbohydrates, nucleic acids, organic molecules, and inorganic biologically active molecules.

The monomers can vary in size and number of functional groups depending upon desired properties for the resulting polymeric material. More particularly, the molecular weight for the monomers can range from about 100 DA to about 60000 Da to about 200000 Da. Prior to formation of the polymeric material of the present invention, the monomers may be derivatized to include thiol or alkyne moieties such that those moieties can participate in radical mediated thiol-ene polymerization. Thiolated macromers such as poly(ethylene glycol) dithiol are available commercially. In another embodiment, cysteine residues in peptides and proteins are used to provide the thiol moiety. The alkyne moieties can be selected from any suitable compound having a carbon-carbon triple bond. For example, the alkyne moiety can be selected from any suitable groups such as hexyne, octyne, hexadiyne, PEG multiyne, and others. Other means for providing thiol moieties and alkynes will be known to those skilled in the art.

The resulting polymers may be formed in the presence of cells and other biological compounds such as proteins and peptides. Furthermore, the monomers may contain hydrophilic and non-hydrophilic regions or elements which add chemical, and / or biological, and / or mechanical functionality.

The resulting polymers can be designed to be degradable if one or more of the co-monomers are chosen to be degradable. As used herein, a polymer is degradable when its rate of degradation is increased by greater than 10% when the polymer is exposed to a degrading agent or process. Degrading agents include chemicals, radiation, heat and enzymes. Degrading processes include photoinitiated chemical processes and mechanical processes.

The polymers described herein can be used as a substrate for the growth of various cell types. These cells can be primary cells or stem cells. These polymers can be used as substrates for cell growth *in vitro* or *in vivo*. The polymers described herein can be used for soft tissue regeneration, bone regeneration, cartilage regeneration, stem manufacture and stem cell delivery.

EXAMPLES

Example 1: Synthesis of alkyne derivatized PEGs.

4-pentynoic acid (1.64 g, 16.7 mmol, Fluka) was added to N,N'-dicyclohexylcarbodiimide (3.44 g, 16.7 mmol, Sigma) and dissolved in minimal dichloromethane (DCM) and stirred overnight under argon. The 4-pentynoic anhydride product was then filtered, concentrated, and added to a solution containing vacuum dried poly(ethylene glycol) (PEG, 5g, 1.67 mmol, Mn ~ 3000, Fluka), pyridine (1.34 mL, 16.7 mmol, Sigma), 4-dimethylaminopyridine (200 mg, 1.67 mmol, Sigma) in minimal DCM and stirred overnight under argon. The crude product was then concentrated, precipitated in diethyl ether, dissolved in deionized water, dialysed for two days and lyophilized to give the desired product.

Similar methods and reagents can be used to form derivatized PEGs of different molecular weight or with a different number of branches. Other methods for producing alkyne derivatized monomers will be readily understood by one skilled in the art. Alkyne derivatized PEGs are also available from commercials sources.

Example 2. Thiol containing PEGs and Peptides.

Thiol derivatized PEG reagents can be purchased from a number of vendors with a variety of molecular weights. To create a degradable thiol-yne polymer, the peptide sequence KCGGYRGCK was synthesized using standard peptide synthesis methods. This chymotrypsin sensitive biscysteine peptide provides two thiol moieties and can be cleaved by the protein chymotrypsin.

Methods for preparing other thiol containing monomers will be readily understood by one skilled in the art.

Example 3. Hydrogel Formation.

10kD 4-Arm PEG Thiol (PEG tetrathiol) was mixed with PEG-3K dialkyne such that the thiol to yne ratio was 1:1. To this was added a 0.8% wt. (36 mM) solution of the photoinitiator Irgacure 2959 in water, such that the final formulation was 13.5% PEG. Polymerization is then initiated by irradiation of the mixture at a wavelength between 300-400nm using a 10mW/cm^2 light source for 1000 seconds.

10kD 4-Arm PEG Thiol (PEG tetrathiol) was mixed with PEG-3K dialkyne such that the thiol to yne ratio was 2:1. To this was added a 0.8% wt. (36 mM) solution of the photo-initiator Irgacure 2959 in water, such that the final formulation was 13.5% PEG. Polymerization is then initiated by irradiation of the mixture at a wavelength of 300-400nm using a 10mW/cm^2 light source for 1000 seconds. In this polymerization reaction, the yne moiety reacts twice with thiol contain moieties – first as the original alkyne and subsequently as a vinyl sulfide.

Example 4: Time course of photochemical polymerization of thiol-yne hydrogels.

In situ dynamic photorheometry was used to demonstrate the photochemical curing of thiol-yne hydrogels (all systems were cured with 0.5 wt % Irgacure 2959 and 10mW/cm^2 365 nm centered UV light). As shown in Figure 1, the elastic modulus of evolving hydrogel networks was plotted against time. Samples were formulated with 2:1 thiol:alkyne of PEG3400 dithiol and PEG10K tetrayne; 2:1, thiol:alkyne chymotrypsin degradable bicysteine peptide and PEG tetrayne (circle); 1:1 thiol:alkyne chymotrypsin degradable bicysteine peptide and PEG tetrayne (triangle); and PEG terayne alone (inverted triangle .

Example 5. Chymotrypsin sensitive FRET substrate.

The sequence KKCBK(FAM)GPQGIWGQK(TAMARA)GCKK was synthesized to yield a biscycteine monomer that generates a FRET signal when cleaved by chymotrypsin . This biscysteine peptide is capable of participating in the thiol-yne polymerization. Cleavage of this peptide by chymotrypsin can be monitored by observing the relative fluorescence when excited with 488 nm light.

Example 6: Formation of degradable hydrogels using the thiol-yne system.

Hydrogels were formed as above using the chymotrypsin sensitive biscysteine peptide and a four arm yne derivatized PEG. In addition the above FRET peptide was included into the monomer mixture, thereby incorporating itself in the network architecture. The resulting hydrogels degraded completely within 1 hour when treated with chymotrypsin at 10mg/ml. Those gels that were not treated with chymotrypsin were stable for longer than 21 days when kept in sterile conditions. Furthermore, the liquid from the degraded hydrogel solution emitted high fluorescence when excited with 488 nm light while an equivalent concentration of the intact FRET substrate emitted little florescence. This indicates that the gel degradation was caused by peptide lysis achieved by the chymotrypsin enzyme (Data shown in Table 1).

Table 1. Fluorescence relative to supernatant from gels not treated with chymotrypsin.

Liquid from non treated gels	1.0±0.2
Liquid from enzyme treated gels	32±2
Liquid with equivalent FRET substrate- no enzyme	3.8±1.2

CLAIMS

1. A composition comprising a polymer comprising two or more types of monomers wherein at least a first monomer comprises at least two thiol moieties and at least a second monomer comprises at least one alkyne moiety and wherein the first and second monomers are crosslinked at bonds between the thiol and alkyne moieties.

2. The composition of claim 1, wherein the first monomer comprises at least 3, 4, 5, 6, 7, 8, 9 or 10 thiol moieties.

3. The composition of claim 1, wherein the second monomer comprises at least 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 alkyne moieties.

4. The composition of claim 1, wherein the first and/or second monomer are derivatized to include a thiol or alkyne moiety.

5. The composition of claim 1, wherein the first and/or second monomer is selected from the group consisting of poly(lactic acid) (PLA), polyglycolide (PGA), copolymers of PLA and PGA (PLGA), poly(vinyl alcohol) (PVA), poly(ethylene glycol) (PEG), poly(ethylene oxide), poly(ethylene oxide)-co-poly(propylene oxide) block copolymers (poloxamers, meroxapols), poloxamines, polyanhydrides, polyorthoesters, poly(hydroxy acids), polydioxanones, polycarbonates, polyaminocarbonates, poly(vinyl pyrrolidone), poly(ethyl oxazoline), carboxymethyl cellulose, hydroxyalkylated celluloses such as hydroxyethyl cellulose and methylhydroxypropyl cellulose, and natural polymers such as nucleic acids, polypeptides, polysaccharides or carbohydrates such as polysucrose, hyaluranic acid, dextran and similar derivatives thereof, heparan sulfate, chondroitin sulfate, heparin, or alginate, and proteins including without limitation gelatin, collagen, albumin, or ovalbumin, or copolymers, or blends thereof. In particularly preferred embodiments, the monomers can be selected from poly(lactic acid) (PLA), poly(vinyl alcohol) (PVA), and poly(ethylene glycol) (PEG).

6. The composition of claim 1, wherein the composition comprises a hydrogel.

7. The composition of claim 5, wherein the hydrogel comprises more than 50% solvent by weight.

8. The composition of claim 8, wherein the hydrogel comprises between 50 and 95% water by weight.

9. The composition of claim 1, wherein the first or second monomers are degradable.

10. The composition of claim 9 , wherein the degradable monomer is hydrolytically, chemically or enzymatically degradable.

11 The composition of claim 1, wherein the first monomer comprises a peptide.

12. The composition of claim 11, wherein the peptide is enzymatically degradable.

13. The composition of claim 12, wherein the enzyme is a protease.

14. The composition of claim 11, wherein the peptide is selected from the group consisting of adhesion peptides (such as RGD adhesion sequence), growth factors, hormones, antihormones, signaling compounds, enzymes, serum proteins, albumins, macroglobulins, globulins, agglutinins, lectins, extracellular matrix proteins, antibodies, and antigens.

15. The composition of claim 1, further comprising an agent that has a biological function or activity.

16. The composition of claim 15, wherein the agent is a peptide selected from the group consisting of adhesion peptides (such as RGD adhesion sequence), growth factors, hormones, antihormones, signaling compounds, enzymes, serum proteins, albumins, macroglobulins, globulins, agglutinins, lectins, extracellular matrix proteins, antibodies, and antigens. Types of non-peptide agents that can be incorporated into the polymeric material include analgesics, antipyretics, nonsteriodal antiinflammatory drugs,

antiallergics, antibacterial drugs, antianemia drugs, cytotoxic drugs, antihypertensive drugs, dermatological drugs, psychotherapeutic drugs, vitamins, minerals, anorexiants, dietetics, antiadiposity drugs, carbohydrate metabolism drugs, protein metabolism drugs, thyroid drugs, antithyroid drugs, and coenzymes.

17. The composition of claim 1, further comprising an agricultural chemical.

18. The composition of claim 17, wherein the agricultural chemical is selected from the group consisting of fungicides, herbicides, fertilizers, pesticides, carbohydrates, nucleic acids, organic molecules, and inorganic biologically active molecules.

19. A method for producing the composition of claim 1 comprising

(a) providing the first and second monomers;

(b) mixing the first and second monomers with a photoinitiator in solvent; and

(c) exposing the first and second monomers and photoinitiator to light, thereby producing the composition of claim 1.

20. The method of claim 19, wherein the photoinitiator is selected from the group consisting of Irgacure 2959, 184 and 651.

21. The method of claim 19, wherein the light is ultraviolet light.

22. The method of claim 21, wherein the ultraviolet light has a wavelength between 300 and 400 nm.

23. The method of claim 19, wherein the exposure to light lasts for less than two, five or 20 minutes.

24. The method of claim 19, wherein the solvent is present at greater than 50% of the mixture of the first and second monomer, photoinitiator and solvent.

25. A method of culturing cells comprising growing the cells on the composition of claim 1.

26. The method of claim 25, wherein the cells are mammalian cells.

27. The method of claim 26, wherein the cells are human cells.

28. The method of claim 25, wherein the cells are primary cells.

29. The method of claim 25, wherein the cells are stem cells.

30. A kit comprising the composition of claim 1.

31. The kit of claim 30, further comprising photoinitiator.

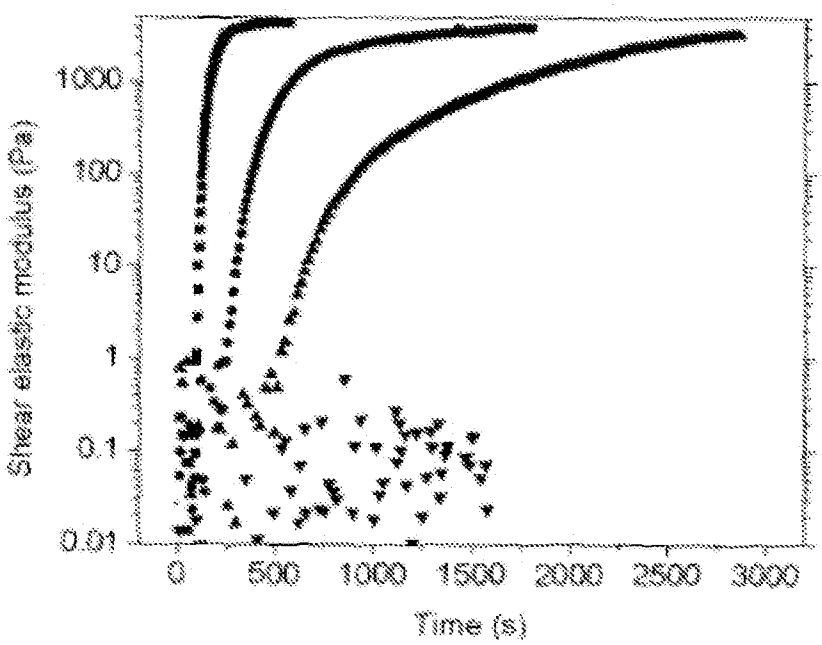
Shear elastic modulus (Pa)
1000
100
10
1
0.1
0.01
0
500
1000
1500
2000
2500
3000
Time (s)

Figure 1