Abstract: A method of introducing a beneficial substance into the body is presented. The method includes the steps of loading the biodendrimer with the beneficial substance, and positioning the biodendrimer relative to the body, such that the beneficial substance can be absorbed by the body.
**DRUG DELIVERY SYSTEM AND METHOD**

**BACKGROUND**

[0001] In order to prevent complications related to ocular treatment, researchers have suggested various implants aimed at localized delivery of anti-angiogenic compounds to the eye. U.S. Pat. No. 5,824,072 to Wong discloses a non-biodegradable polymeric implant with a pharmaceutically active agent disposed therein. The pharmaceutically active agent diffuses through the polymer body of the implant into the target tissue. The pharmaceutically active agent may include drugs for the treatment of macular degeneration and diabetic retinopathy. The implant is placed substantially within the tear fluid upon the outer surface of the eye over an avascular region, and may be anchored in the conjunctiva or sclera; episclerally or intrasclerally over an avascular region; substantially within the suprachoroidal space over an avascular region such as the pars plana or a surgically induced avascular region; or in direct communication with the vitreous.

[0002] U.S. Pat. No. 5,476,511 to Gwon et al. discloses a polymer implant for placement under the conjunctiva of the eye. The implant may be used to deliver neovascular inhibitors for the treatment of ARMD and drugs for the treatment of retinopathies, retinitis, and CMV retinitis. The pharmaceutically active agent diffuses through the polymer body of the implant.

[0003] U.S. Pat. No. 5,773,019 to Ashton et al. discloses a non-bioerodable polymer implant for delivery of certain drugs including angiostatic steroids and drugs such as cyclosporine for the treatment of uveitis. Once again, the pharmaceutically active agent diffuses through the polymer body of the implant.

[0004] All of the above-described implants require careful design and manufacture to permit controlled diffusion of the pharmaceutically active agent through a polymer body (matrix devices) or polymer membrane (reservoir devices) to the desired site of therapy. Drug release from these devices depends on the porosity and diffusion characteristics of the matrix or membrane, respectively. These parameters must be tailored for each drug moiety to be used with these devices. Consequently, these requirements generally increase the complexity and cost of such implants. U.S. Pat. No. 5,824,073 to Peyman discloses an indentor for positioning in the eye. The indentor
has a raised portion that is used to indent or apply pressure to the sclera over the macular area of the eye. This patent discloses that such pressure decreases choroidal congestion and blood flow through the subretinal neovascular membrane, which, in turn, decreases bleeding and subretinal fluid accumulation.

SUMMARY

[0005] A method of introducing a beneficial substance into the body is presented. The method includes the steps of loading biodendrimer with the beneficial substance and positioning the biodendrimer relative to the body, such that the beneficial substance can be absorbed by the body.

[0006] A device for introducing a beneficial substance into the body is also presented. The device includes a first substance including biodendrimer, and a second substance that has properties beneficial to the body.

[0007] A lens for altering the refractive properties of the eye is also presented. The lens includes a first material including biodendrimer, and a second material adapted to change the shape of the lens when exposed to an energy source.

[0008] Additional features and advantages of the present invention are described in, and will be apparent from, the following Detailed Description of the Invention and the figures.

BRIEF DESCRIPTION OF THE FIGURES

[0009] Fig. 1 is a side elevational view in section taken through the center of an eye showing the cornea, pupil, crystalline lens, and capsular bag.

[0010] Fig. 2 is a side elevational view in section of the eye shown in Fig. 1 showing the capsular bag after removal of the crystalline lens.

[0011] Fig. 3 is a side elevational view in section of the eye shown in Fig. 2 showing the treatment of the interior of the capsular bag with a liquid to prevent capsular opacification.

[0012] Fig. 4 is a side elevational view in section of the eye shown in Fig. 3 showing the injection of a synthetic material with free monomers into the capsular bag using a fiber optic tube.
[0013] Fig. 5 is a side elevational view in section of the eye shown in Fig. 4 showing the removal of the fiber optic tube and curing of the injected material at the injection site to form an artificial lens.

[0014] Fig. 6 is a side elevational view in section of the eye shown in Fig. 5 showing the adjustment of the artificial lens using a laser.

[0015] Fig. 7 is a side elevational view in section of the eye shown in Fig. 5 in which the central area of the artificial lens has increased in volume in response to the application of the light.

[0016] Fig. 8 is a side elevational view in section of the eye shown in Fig. 5 in which the peripheral area of the artificial lens has increased in volume in response to the application of the light.

[0017] Fig. 9 is a side elevational view in section of the eye shown in Fig. 5 in which an anterior capsulotomy has been performed to allow the central area of the artificial lens to expand.

[0018] Fig. 10 is a side elevational view of another embodiment of the present invention, wherein an artificial capsular bag is inserted into the natural capsular bag.

[0019] Fig. 11 is a side elevational view of an embodiment of the present invention, wherein only the rear portion of the intraocular lens has been polymerized.

[0020] Fig. 12 is a side elevational view of the embodiment of Fig. 11 showing a portion of the intraocular lens increasing in volume when exposed to laser light.

[0021] Fig. 13 is a side elevational view of the embodiment of Fig. 11 showing a portion of the intraocular lens decreasing in volume when exposed to laser light.

[0022] Fig. 14 is a side elevational view of an embodiment of the present invention, wherein the interior of the artificial bag is divided into two portions.

[0023] Fig. 15 is a side elevational view of the embodiment of Fig. 14 showing the insertion of a liquid into one the interior chambers of the artificial bag.

[0024] Fig. 16 is a side elevational view of the embodiment of Fig. 14 showing a portion of the intraocular lens increasing in volume when exposed to laser light.

[0025] Fig. 17 is a side elevational view of the embodiment of Fig. 14 showing a portion of the intraocular lens decreasing in volume when exposed to laser light.

[0026] Fig. 18 is a side elevational view of the embodiment of Fig. 14 showing accommodation.
[0027] Fig. 19 is a side elevational view of an embodiment of the present invention, wherein a portion of the interior of the capsular bag is coated and the remainder of the capsular bag is filled with biodendrimer or a mixture of biodendrimer and at least one other material.

[0028] Fig. 20 is a side elevational view of an embodiment of the present invention, wherein an artificial lens is inserted into the capsular bag and the remainder of the capsular bag is filled with biodendrimer or a mixture of biodendrimer and at least one other material.

[0029] Fig. 21 is a side elevational view of an embodiment of the present invention, wherein an exterior surface of the capsular bag is coated with biodendrimer or a mixture of biodendrimer and at least one other material.

[0030] Fig. 22 is a side elevational view of an embodiment of the present invention, wherein a portion of the crystalline lens of an eye is removed and replaced with biodendrimer or a mixture of biodendrimer and at least one other material.

[0031] Fig. 23 is a side elevational view of another embodiment of the present invention, wherein a mixture of biodendrimer and at least one other beneficial material is loaded into the eye.

[0032] Fig. 24 is a flow diagram of a method of forming and reloading a biodendrimer carrier system.

[0033] Fig. 25 is a side elevation view in section of a biodendrimer lens that has a second material mixed therein, so that the refractive properties of the contact lens can be altered.

[0034] Fig. 26 is side elevational view of a biodendrimer contact lens that has a second material attached thereto, so that the refractive properties of the contact lens can be altered.

[0035] Fig. 27 is a side elevational view in section of the lens of Fig. 26 with the refractive properties being altered via a laser.

[0036] Fig. 28 is a side elevational view of a biodendrimer contact lens that has a second material inserted into a recession, so that the refractive properties of the contact lens can be altered.
DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

[0037] Referring initially to Fig. 1, a normal eye 10 has a cornea 12, an iris 14, and a crystalline lens 16. The crystalline lens 16 is contained within a capsular bag 18 that is supported by zonules 20. The zonules 20, in turn, are connected to the ciliary muscle 22. According to Helmholtz's theory of accommodation, upon contraction of the ciliary muscle 22, the tension on the zonules 20 is released. The elasticity of the lens causes the curvature of the lens 16 to increase, thereby providing increased refractive power for near vision. Conversely, during dis-accommodation, the ciliary muscle 22 is relaxed, increasing the tension on the zonules 20 and flattening the lens 16 to provide the proper refractive power for far vision.

[0038] To replace the crystalline lens in accordance with the method of the present invention, the first step is to remove the existing lens. Preferably, one or more of the materials that replace the crystalline lens include biodendrimer. As illustrated in Fig. 2, the lens is removed using any technique which allows removal of the lens through a relatively small incision, preferably about a 1-2 mm incision. The preferred method is to create a relatively small incision 24 in the cornea 12 and then perform a capsulorhexis to create an opening 26 into the anterior side 28 of the capsular bag 18. An ultrasonic probe 30 is inserted into the capsular bag 18 through the opening 26. The probe's vibrating tip 32 emulsifies the lens 16 into tiny fragments that are suctioned out of the capsular bag by an attachment on the probe tip (not shown). Alternatively, the lensectomy may be performed by laser phacoemulsification or irrigation and aspiration.

[0039] Once the crystalline lens 16 has been removed, the capsular bag 18 is treated to help prevent a phenomenon known as capsular opacification. Capsular opacification is caused by the proliferated growth of the epithelial cells on the lens capsule. This growth can result in the cells covering all or a substantial portion of the front and rear surfaces of the lens capsule, which can cause the lens capsule to become cloudy and thus adversely affect the patient's vision. These cells can be removed by known techniques, such as by scraping away the epithelial cells; however, it is often difficult to remove all of the unwanted cells. Furthermore, after time, the unwanted cells will typically grow back, requiring further surgery. To prevent capsular opacification, the
capsular bag 18 is treated to eliminate the proliferated growth of epithelial cells, as described below.

[0040] As seen in Fig. 3, one method of treating the epithelial cells to prevent capsular opacification is to use a cannula 34 to introduce a warm liquid 36 (preferably about <60° C) into the capsular bag 18, filling the capsular bag 18. The liquid contains a suitable chemical that kills the remaining lens cells in the capsular bag and also cleans the interior of the capsular bag. Suitable chemicals, as well as other suitable methods of treatment that prevent capsular opacification are disclosed in U.S. Patent No. 6,673,067 to Peyman, which is herein incorporated by reference in its entirety.

[0041] After treating the capsular bag to prevent capsular opacification, the capsular bag is filled with a synthetic, injectable material. The synthetic material is preferably a silicone based material which is un-polymerized. The material has a viscosity between about 10 centistokes (cSt) and 10,000 centistokes at body temperature (or about 37° C) so that it may be injected into the body though a cannula. The synthetic material contains loose monomers and an initiator that initiates polymerization of the loose monomers. In a preferred embodiment, the initiator is a photoinitiator so that when the material is exposed to the proper wavelength of light, preferably blue light, the initiator causes the loose monomers to polymerize. Initiators responsive to other sources of energy, such as heat or chemicals, may be used if desired.

[0042] The polymerization of the monomers caused by the initiators results in a lower concentration of monomers in the polymerized area. Through the principle of diffusion, loose monomers therefore migrate to the polymerized area, causing the polymerized area to swell. Suitable materials, and a more detailed discussion of their method of operation, are disclosed in U.S. Pat. No. 6,721,043 B2 to Platt et al., U.S. Pat. No. 6,749,632 B2 to Sandstedt et al., and U.S. Pat. App. No. 2003/0174375 A1 to Jethmalani et al, all of which are herein incorporated by reference in their entirety.

[0043] As shown in Fig. 4, the synthetic material 38 is injected into the capsular bag 18 using a hollow tube 40. The synthetic material 38 is preferably a mixture that includes biodendrimer and an un-polymerized material; however, the synthetic material 38 can be any suitable material. Preferably, the un-polymerized material is an un-polymerized silicone based material; however, the material can be any suitable un-polymerized material. Further, the synthetic material 38 is preferably a mixture of
approximately 50% biodendrimer and approximately 50% an un-polymerized material; however, the synthetic material 38 can have any suitable percentage of biodendrimer, un-polymerized material or other material.

[0044] It should be noted that the biodendrimer can be loaded with a beneficial substance as described herein.

[0045] Returning to Fig. 4, preferably, the tube 40 is a hollow fiber optic (i.e. light conducting) tube and the injection is made through the same opening 26 that was created to remove the crystalline lens 16. The amount of material that is injected into the capsular bag is chosen so that it closely approximates the desired refractive power of the original, natural lens. Any remaining fluid that is present in the capsular bag prior to injection of the synthetic material 38 can either be aspirated through another hole in the capsular bag, or can simply be allowed to leak through the edges of the capsular bag.

[0046] After the desired amount of material has been injected into the capsular bag 18, light 41 is transmitted through the light conducting tube 40 at the same time the tube is withdrawn from the opening 26 to the capsular bag 18. The light 41 is at the appropriate wavelength to initiate polymerization of the liquid material. Thus, when the tube 40 is removed, the polymerized liquid material forms a polymerized plug 42 that seals the opening 26 into the capsular bag 18, trapping the remaining liquid material inside the capsular bag. It should be noted that the liquid material can be polymerized in any suitable manner. At this point, the capsular bag 18 is filled with a liquid, photo-sensitive material, thereby forming an artificial lens 44.

[0047] After creating the artificial lens 44, a suitable period of time, such as a few minutes, hours or days, is allowed to elapse so that the eye heals and the refractive power of the eye stabilizes. The eye is then measured to determine if there are any remaining optical aberrations in the eye that need to be corrected. The eye can be measured using, for example, wavefront sensor technology. If there are any errors which need to be corrected, the artificial lens 44 can be adjusted by exposing the lens 44 to light 46, which is generated by a light source 48 (Fig. 6). Light 46 is applied in a predetermined pattern to modify the refractive properties of the lens 44 as desired to create perfect, or 20/20, far vision.
For example, referring to Fig. 7, if the surgeon determines that additional plus dioptic power is needed, the surgeon can selectively polymerize the central portion 50 of the artificial lens 44 by aiming a light with the appropriate wavelength through the cornea 12 towards the central portion 48 of the lens. As discussed above, this will cause the central portion 48 of the lens to swell, thereby providing increased plus dioptic power. Conversely, if the surgeon wishes to lower the plus dioptic power of the lens, the surgeon can direct blue light towards the periphery 52 of the lens. This will cause the periphery 52 to swell, thereby flattening the lens 44 and reducing the amount of plus dioptic power of the lens 44. Likewise, various portions of the lens may be irradiated with the light to introduce corrections for other optical aberrations, such as astigmatisms.

The adjustment process may be repeated until the desired corrective capabilities have been programmed into the lens 44. Once satisfied with the lens, the entire lens 44 is irradiated with an appropriate wavelength of light to polymerize the entire unpolymerized material in the lens, thereby fixing the refractive power of the lens.

After this final polymerization of the lens, the lens 44 takes on a gel-like consistency that approximates the function of a crystalline lens. The lens 44 therefore is capable of providing accommodation. That is, in the method of the present invention, the capsular bag 18 has been left substantially intact, and the zonules 20 and ciliary muscle 22 have not been damaged. Consequently, upon contraction or relaxation of the ciliary muscle 22, the artificial lens 44 functions like a natural lens, since the polymerized material has a gel-like consistency. Therefore, lens 44 can become rounder or flatter like a natural lens to provide accommodation for near vision.

Furthermore, accommodation takes place because the contraction and relaxation of the ciliary muscle 22 moves the lens forward and backward (i.e. closer to and further from the retina). This movement of the lens also produces accommodation.

Fig. 9 shows an additional method of changing the refractive power of the implanted artificial lens 44. In Fig. 9, after the lens 44 has been polymerized to a gel-like consistency, an anterior capsulotomy is performed to remove the central portion of the anterior side 28 of the capsular bag 18. This allows the gel-like lens 44 to bulge
slightly forward through the capsulotomy 54 to add additional dioptic power to the lens during accommodation.

[0053] Figs. 10-18 show an another embodiment of the present invention, wherein an IOL 59, which preferably includes biodendrimer which may be unloaded or loaded biodendrimer as described above, is formed by an artificial capsular bag or capsule 60 that is positioned within the original or natural capsular bag 18.

[0054] This artificial capsular bag 60 is preferably formed from biodendrimer, unloaded or loaded as described above, or a mixture of biodendrimer and at least one other material; however, artificial bag 60 can be formed from silicon or any other suitable transparent polymer. Preferably, when biodendrimer is used, it is approximately 50% of the mixture; however, the biodendrimer can be any suitable percentage of the mixture. Artificial bag 60 is adapted to allow light within the visible spectrum to pass therethrough. Preferably, capsular bag or capsule 60 has an exterior surface 62 and an interior surface 64, which defines an interior area or portion 66. Interior portion 66 can extend through the entire bag 60 or occupy a limited portion thereof. For example, portion 66 can be located in the rear portion of the bag, the front portion of the bag, the top portion of the bag, or the bottom portion of the bag or any other suitable location. Each location of portion 66 (i.e., rear, front, top and bottom) is relative to the location of a natural human eye, and is merely used herein for ease of understanding and is not meant to limit the present invention in any manner.

[0055] Additionally, portion 66 can occupy any percentage of the bag - i.e., substantially about 100% to substantially about 1%. The remainder of the bag can be filled with any suitable material, as described above, below, or in Application Serial No. 10/272,402, discussed above, or merely be defined by the thickness of the wall 68 between the exterior surface 62 and the interior surface 64. For example, the remainder of the bag can be filled with biodendrimer, a mixture of biodendrimer and at least one other material, or any other suitable material. Preferably, biodendrimer is approximately 50% of the mixture; however, the biodendrimer can be any suitable percentage of the mixture. Further, the biodendrimer can be loaded as described above.

[0056] As shown specifically in Fig. 10, the central portion 69 of the natural capsular bag along the main optical axis is removed. The artificial capsular bag 60 is then
inserted into the natural capsular bag 18 through opening 70. The artificial bag 60 can be placed inside of the natural bag 18 in any manner desired. For example, bag 60 can be merely positioned within bag 18, it can be positioned in bag 18 such that bag 18 is slightly stretched, it can be positioned, such that there is a "tight" fit (i.e., the artificial bag is tightly held within the natural bag, such that there is sufficient friction that the artificial bag cannot move or only move an insubstantial amount), or the artificial lens can be positioned with the natural bag using haptics any other type of device to prevent movement thereof. Further, the artificial bag 60 can be placed inside of the natural bag 18 such that there is space between some or the entire artificial bag 60 and the natural bag 18. Preferably, the space is filled with biodendrimer; however, the space can be filled with a mixture of biodendrimer and at least one other material, or any other suitable material, or left vacant if desired. Preferably, if a mixture occupies the space, biodendrimer is approximately 50% of the mixture; however, the biodendrimer can be any suitable percentage of the mixture. Further, the biodendrimer can be loaded as described above.

[0057] By removing the central portion 69 of the natural capsular bag to form opening 70, the natural lens along the main optical axis is removed. This eliminates or substantially eliminates the possibility of capsular opacification of the lens in this area. However, it is noted that it is not necessary to remove the portion of the capsular bag at the main optical axis, and any size opening or aperture can be formed in any portion of the natural capsular bag that enables an artificial bag to be placed therein.

[0058] The capsular bag 60 is then filled with a liquid or synthetic material 72, which preferably includes monomers and a polymerization initiator, such as a photosensitizer in the same or substantially similar manner as the method and system described above for original capsular bag 18. Material 72 does not necessarily need to include both monomers and a photosensitizer, and may include only monomers or a photosensitizer, or any other material(s) that would enable the material to polymerize and/or change shape and/or volume. For example, material 72 can be biodendrimer or a mixture of biodendrimer and at least one other material. Preferably, biodendrimer is approximately 50% of the mixture; however, the biodendrimer can be any suitable percentage of the mixture. Further, the biodendrimer can be loaded as described
above. It is noted that the capsular bag 60 does not necessarily need to be filled after placement in the natural capsular bag and can be filled at any suitable time.

[0059] The synthetic material 72 is preferably the same of substantially similar to the materials described above or any material described in above mentioned U.S. Application Serial No. 10/272,402, the contents of which have previously been incorporated herein by reference. For example, the synthetic material 72 preferably contains loose monomers and an initiator that initiates polymerization of the loose monomers. In a preferred embodiment, the initiator is a photoinitiator so that when the material is exposed to the proper wavelength of light, preferably blue light, the initiator causes the loose monomers to polymerize. Initiators responsive to other sources of energy, such as heat or chemicals, may be used if desired.

[0060] The polymerization of the monomers caused by the initiators results in a lower concentration of monomers in the polymerized area. Through the principle of diffusion, loose monomers therefore migrate to the polymerized area, causing the polymerized area to swell. This allows the IOL to be adjusted to create perfect or substantially perfect (i.e., 20/20) vision. Suitable materials, and a more detailed discussion of their method of operation, are disclosed in U.S. Pat. No. 6,721,043 B2 to Platt et al, U.S. Pat. No. 6,749,632 B2 to Sandstedt et al, and U.S. Pat. App. No. 2003/0174375 A1 to Jethnialani et al, all of which are herein incorporated by reference in their entirety.

[0061] As described in the previous embodiments, changing the volume of the IOL 59 can result in a decrease or in increase in volume, thus changing the refractive properties of the lens to increase or decrease the diopter power. Additionally, the IOL can be adjusted multiple times as described above to "fine tune" the refractive properties of the IOL. Once the IOL has the desired refractive properties, the IOL can be completely polymerized as described above.

[0062] Additionally, as shown in Fig. 11, a portion 74, such as the rear portion of liquid or material 72, can be polymerized prior to insertion inside of the natural capsular bag 18. However, it is noted that the portion 74 to be polymerized does not necessarily need to be the rear portion and can be any portion desired, including a front portion or a front and rear portion. By polymerizing portion 74 prior to insertion into capsular bag 18, the artificial bag 60 has rigidity that can help shape and/or support the
natural bag in a predetermined manner, thus facilitating the forming of the desired shape of the natural and/or artificial bags.

[0063] Furthermore, portion 74 need not necessarily be a liquid that is polymerized as discussed above, but can be a solid or substantially solid material that is generally used for forming conventional IOLs or any other suitable material. For example, portion 74 can be a separate collagen material (or any other suitable material) added to the interior or exterior of the bag or it may simply by a portion of wall between the exterior surface 62 and the interior surface 64. Further, portion 74 can be biodendrimer or a mixture of biodendrimer and at least one other material. Preferably, biodendrimer is approximately 50% of the mixture; however, the biodendrimer can be any suitable percentage of the mixture. Further, the biodendrimer can be loaded as described above.

[0064] Additionally, the capsular bag 60 can be positioned adjacent to or coupled to a conventional IOL. For example, the capsular bag 60 can affixed to the front surface or rear surface of a conventional IOL prior to, during or after insertion of the IOL in the natural capsular bag 18.

[0065] As shown in Figs. 12 and 13, and as discussed above, changing the volume of the front portion of the IOL 59 by exposing the unpolymerized material to a light (such as from laser 75 or any other suitable light source) will result in a decrease or an increase in volume, thus changing the refractive properties of the lens to increase or decrease the diopter power. Additionally, the IOL can be adjusted multiple times as described above to "fine tune" the refractive properties of the IOL. Once the IOL has the desired refractive properties, the IOL can be completely polymerized as described above. It is noted that as with the other embodiments described above and in Application Serial No. 10/272,402, the polymerizing initiator can initiate polymerization when exposed to light, laser light, a chemical or any other suitable device and/or method.

[0066] Additionally, as shown in Fig. 14, the artificial capsular bag 60 can be divided into two interior portions, a first portion or chamber 76 and a second portion or chamber 78. Preferably, first portion 76 is located in the front part of bag 60 (i.e., closer to the anterior chamber or the iris) and second portion 78 is located in the rear or back portion of the bag (i.e., farther from the anterior chamber of iris).
Prior to insertion into the natural bag 18, the rear chamber preferably is filled with liquid or material 80, which preferably includes monomers and a polymerization initiator, such a photosensitizer in the same or substantially similar manner as the method and system described above for each of the other embodiments. Liquid 80 does not necessarily need to include both monomers and a photosensitizer, and may include only monomers or a photosensitizer, or any other material that would enable the material to polymerize and or change shape and/or volume. Further, liquid 80 can be biodendrimer or a mixture of biodendrimer and at least one other material. Preferably, biodendrimer is approximately 50% of the mixture; however, the biodendrimer can be any suitable percentage of the mixture. Further, the biodendrimer can be loaded as described above.

As shown in Fig. 15, the front chamber is preferably filled with a liquid polymer or material 82 suitable for insertion into the eye using a cannula 85 or any other suitable method or device. The liquid polymer can be inserted into chamber 76 through an opening 83 or a small self sealing membrane after implantation of the bag 60. It is noted that both liquid 80 and liquid 82 can be inserted into the bag at any time desired. For example, each liquid can be inserted before, after or during the surgical procedure. Liquid 82 can be biodendrimer or a mixture of biodendrimer and at least one other material. Preferably, biodendrimer is approximately 50% of the mixture; however, the biodendrimer can be any suitable percentage of the mixture. Further, the biodendrimer can be loaded as described above.

It is noted that it is not necessary to fill the rear chamber with liquid 80 and the front chamber with liquid 82. This positioning of the respective liquids is merely the preferred embodiment and either of the liquids can be placed in either of the chambers. Furthermore it is noted that chambers 76 and 78 can have substantially the same volume or can have any volume desired. For example, one chamber can be larger or smaller than the other volume. Additionally, the overall volume of both chambers can occupy any amount of the volume of IOL 59 desired. For example the overall volume of chambers 76 and 78 can occupy from about 1% of the overall volume for IOL 59 to about 99%.

As shown in Figs. 16 and 17, and as discussed above, changing the volume of the rear chamber 78 of the IOL 59 by exposing the unpolymerized material to a light
(such as from laser 75 or any other suitable light source) will result in a decrease or an increase in volume, thus changing the refractive properties of the lens to increase or decrease the diopter power. Additionally, the IOL can be adjusted multiple times as described above to "fine tune" the refractive properties of the IOL. Once the IOL has the desired refractive properties, the IOL can be completely polymerized as described above. It is noted that as with the other embodiments described above and in Application Serial No. 10/272,402, the polymerizing initiator can initiate polymerization when exposed to light, laser light, a chemical or any other suitable device and/or method.

[0071] As shown in Fig. 18, this embodiment allows the lens system, particularly the bag 60 to remain flexible, and thus act like a natural lens. In other words, when the eye attempts to focus on a near object (i.e., accommodate), the lens zonules loosen the natural bag, which in turn loosens the artificial bag. Each bag 18 and 60 then bulges slightly in the center. This bulging increases the refractive power of the natural lens. Conversely when the zonules tighten, each bag tends to be stretched, decreasing the refractive power. That is, when a portion of the artificial bag 60 is filled with liquid polymer 82, the artificial bag 60 and thus the natural bag 18 remain flexible after implantation. Therefore, the process of accommodation bulges the central portion of the bag, which increases the convexity of the front portion of the lens, increasing the refractive power of the lens for near vision.

[0072] Additionally, since the liquid is a polymer any exposure to light or a polymerizing agent does not polymerize the this material; however, as described above, the material 80 can be subject to exposure to different energies that would increase or decrease the volume and/or polymerize a portion or the entire volume thereof, as for any of the embodiments describe above or in application serial no. 10. 10/272,402.

[0073] Furthermore, the rear chamber or portion 78 can be divided into two areas or portions in a manner similar to the embodiment described in Figs. 11-13 and Figs. 14-18, thus forming three chambers or areas with the artificial bag 60. In this embodiment, a first portion would be filled with a material, such as liquid 82, the second portion would be filled with a material, such as material 80, and the third portion would include a polymerized material as described from Figs. 11-13. Therefore
as described above, the lens can have rigidity for insertion into the capsular bag 18 and have the volume thereof changed while inside the capsular bag to achieve the desired refractive power.

[0074] Fig. 19 shows another embodiment of the present invention, wherein an IOL 84 is formed by coating a portion 86 of capsular bag 18 with a synthetic material 88. The synthetic material 88 is preferably a silicone based material which is un-polymerized as described above and shown in Fig. 4; however, the synthetic material 88 can be any suitable material. Preferably, the synthetic material 88 contains loose monomers and an initiator that initiates polymerization of the loose monomers. In a preferred embodiment, the initiator is a photoinitiator so that when the material is exposed to the proper wavelength of light, preferably blue light, the initiator causes the loose monomers to polymerize. Initiators responsive to other sources of energy, such as heat or chemicals, may be used if desired.

[0075] As above, the polymerization of the monomers caused by the initiators results in a lower concentration of monomers in the polymerized area. Through the principle of diffusion, loose monomers therefore migrate to the polymerized area, causing the polymerized area to swell. Some suitable materials, and a more detailed discussion of their method of operation, are disclosed in U.S. Pat. No. 6,721,043 B2 to Platt et al., U.S. Pat. No. 6,749,632 B2 to Sandstedt et al., and U.S. Pat. App. No. 2003/0174375 A1 to Jethmalani et al, all of which were incorporated by reference in their entirety above.

[0076] It should be noted that though Fig. 19 shows portion 86 of capsular bag 18 being a rear portion, any portion, including but not limited to the front, top, bottom, sides, or any combination thereof, can be coated with synthetic material 88. The portion 86 of capsular bag 18 can be coated using any suitable method, including but not limited to injection though a cannula.

[0077] The space 90 within the capsular bag 18 after the portion 86 is coated is preferably filled with biodendrimer 92; however, the space 90 can be filled with a mixture of biodendrimer and at least one other material. If the space 90 is filled with a mixture of biodendrimer and at least one other material, biodendrimer is preferably approximately 50% of the mixture; however, biodendrimer can be any suitable percentage of the mixture. Further, the biodendrimer can be loaded as described
above. The space 90 can be filled with biodendrimer 92 using any suitable method, including but not limited to injection though a cannula.

[0078] As discussed above, the refractive properties of IOL 84 can be altered by changing the volume of the portion 86 of the IOL 84 by exposing the unpolymerized material to a light. Additionally, the IOL 84 can be adjusted multiple times as described above to "fine tune" the refractive properties of the IOL 84. Once the IOL has the desired refractive properties, the IOL can be completely polymerized as also described above. It is noted that as with the other embodiments described above and in Application Serial No. 10/272,402, the polymerizing initiator can initiate polymerization when exposed to light, laser light, a chemical or any other suitable device and/or method.

[0079] Similar to other embodiments, this embodiment allows the lens system to remain flexible, and thus act like a natural lens. In other words, when the eye attempts to focus on a near object (i.e., accommodate), the lens zonules loosen the capsular bag 18. The bag 18 then bulges slightly in the center, and this bulging increases the refractive power of the natural lens. Conversely when the zonules tighten, the bag tends to be stretched, decreasing the refractive power. That is, when a space 90 of the capsular bag 18 is filled with biodendrimer 92, or a mixture of biodendrimer and at least one other suitable material, the capsular bag 18 remains flexible after implantation of IOL 84. Therefore, the process of accommodation bulges the central portion of the bag 18, which increases the convexity of the front portion of the lens, increasing the refractive power of the lens for near vision.

[0080] Fig. 20 shows still another embodiment of the present invention, wherein an IOL 94 is formed by inserting an artificial lens 96 into the capsular bag 18. The artificial lens 96 is preferably silicone based; however, the artificial lens 96 can be any suitable material, including biodendrimer, which can be unloaded or loaded as described above. Preferably, the artificial lens 96 includes loose monomers and an initiator that initiates polymerization of the loose monomers. In a preferred embodiment, the initiator is a photoinitiator so that when the material is exposed to the proper wavelength of light, preferably blue light, the initiator causes the loose monomers to polymerize. Initiators responsive to other sources of energy, such as heat or chemicals, may be used if desired.
[0081] As above, the polymerization of the monomers caused by the initiators results in a lower concentration of monomers in the polymerized area. Through the principle of diffusion, loose monomers therefore migrate to the polymerized area, causing the polymerized area to swell. Some suitable materials, and a more detailed discussion of their method of operation, are disclosed in U.S. Pat. No. 6,721,043 B2 to Platt et al., U.S. Pat. No. 6,749,632 B2 to Sandstedt et al., and U.S. Pat. App. No. 2003/0174375 A1 to Jethmalani et al, all of which were incorporated by reference in their entirety above.

[0082] It should be noted that though Fig. 20 shows the artificial lens 96 being placed in the center of the capsular bag 18, the artificial lens can be placed in any location within the capsular bag 18, including but not limited to the front or back. Preferably, the artificial lens 96 is placed in the capsular bag 18 by rolling or folding the lens 96 and inserting the lens 96 though an opening in the capsular bag 18; however, the lens 96 can be inserted using any suitable technique. Once inside the bag 18, the lens 96 preferably unrolls or unfolds automatically; however, the lens 96 can be unrolled or unfolded manually, if desired. Preferably, the lens is sized and configured to frictionally fit within the capsular bag, such that the lens is immobile or substantially immobile; however the lens can be positioned and/or fixed in position in any suitable manner.

[0083] The space 98 within the capsular bag 18 after the lens 96 is inserted is preferably filled with biodendrimer 100; however, the space 98 can be filled with a mixture of biodendrimer and at least one other material. If the space 98 is filled with a mixture of biodendrimer and at least one other material, biodendrimer is preferably approximately 50% of the mixture; however, biodendrimer can be any suitable percentage of the mixture. The space 98 can be filled with biodendrimer 100 using any suitable method, including but not limited to injection though a cannula. Further, the biodendrimer can be loaded as described above.

[0084] As discussed above, the refractive properties of IOL 94 can be altered by changing the volume of the lens 96 of the IOL 94 by exposing the unpolymerized material to a light. Additionally, the IOL 94 can be adjusted multiple times as described above to “fine tune” the refractive properties of the IOL 94. Once the IOL has the desired refractive properties, the IOL can be completely polymerized as also
described above. It is noted that as with the other embodiments described above and in Application Serial No. 10/272,402, the polymerizing initiator can initiate polymerization when exposed to light, laser light, a chemical or any other suitable device and/or method.

[0085] Similar to other embodiments, this embodiment allows the lens system to remain flexible, and thus act like a natural lens. In other words, when the eye attempts to focus on a near object (i.e., accommodate), the lens zonules loosen the capsular bag 18. The bag 18 then bulges slightly in the center, and this bulging increases the refractive power of the natural lens. Conversely when the zonules tighten, the bag tends to be stretched, decreasing the refractive power. That is, when a space 98 of the capsular bag 18 is filled with biodendrimer 100, or a mixture of biodendrimer and at least one other suitable material, the capsular bag 18 remains flexible after implantation of IOL 94. Therefore, the process of accommodation bulges the central portion of the bag 18, which increases the convexity of the front portion of the lens, increasing the refractive power of the lens for near vision.

[0086] Fig. 21 shows still another embodiment of the present invention, wherein an IOL 102 is formed by coating the exterior of the capsular bag 18 with a synthetic material 104. The synthetic material 104 is preferably a mixture that includes biodendrimer and an un-polymerized material; however, the synthetic material 104 can be any suitable material. Preferably, the un-polymerized material is an un-polymerized silicone based material; however, the material can be any suitable un-polymerized material. Further, the synthetic material 104 is preferably a mixture of approximately 50% biodendrimer and approximately 50% an un-polymerized material; however, the synthetic material 104 can have any suitable percentage of biodendrimer, un-polymerized material or other material. Further, the biodendrimer can be loaded as described above.

[0087] The synthetic material 104 can be selectively polymerized, as discussed above, to adjust the optical properties of the eye. The adjustment process can be repeated until the desired corrective capabilities have been programmed into the lens 102. Once satisfied with the optical properties, the entire lens 102 is irradiated with an appropriate wavelength of light to polymerize the entire un-polymerized material in the lens, thereby fixing the refractive power of the lens 102.
After this final polymerization of the lens 102, the lens 102 takes on a gel-like consistency that approximates the function of a crystalline lens. The lens 102 therefore is capable of providing accommodation. It should be noted that removal of the original crystalline lens is not necessary for formation of the IOL 102 by coating the exterior of the capsular bag 18 with the synthetic material 104.

Fig. 22 shows still another embodiment of the present invention, wherein an IOL 106 is formed by removing only a portion of the crystalline lens 16. The portion can be removed using any suitable technique, including but not limited to the techniques described above for removing the entire crystalline lens. Once the portion is removed, the remaining cavity is at least partly filled with a synthetic material 108. The synthetic material 108 is preferably a mixture that includes biodendrimer and an un-polymerized material; however, the synthetic material 108 can be any suitable material. Preferably, the un-polymerized material is an un-polymerized silicone based material; however, the material can be any suitable un-polymerized material, including biodendrimer, which can be unloaded or loaded as described above. Further, the synthetic material 108 is preferably a mixture of approximately 50% biodendrimer and approximately 50% un-polymerized material; however, the synthetic material 108 can have any suitable percentage of biodendrimer, un-polymerized material or other material. Further, the biodendrimer can be loaded as described above.

The synthetic material 108 can be selectively polymerized, as discussed above, to adjust the optical properties of the eye. The adjustment process can be repeated until the desired corrective capabilities have been programmed into the lens 106. Once satisfied with the optical properties, the entire lens 106 is irradiated with an appropriate wavelength of light to polymerize the entire unpolymerized material in the lens, thereby fixing the refractive power of the lens 106. After this final polymerization of the lens 106, the lens 106 retains the ability to accommodate.

Fig. 23 illustrates another embodiment of the present invention wherein a substance or carrier 150 is inserted or injected into eye 10 using a syringe 152. Substance 150 preferably includes biodendrimer and a beneficial substance. The substance 150 can then be shaped, smoothed or merely left untouched after insertion under the conjunctive. The substance is preferably loaded, impregnated, or otherwise associated with one or more drugs, medications, vitamins, nutrients and/or any other
therapeutic or beneficial substance. For example, the beneficial substance can be any one, at least one or combination of the following substances: anti-inflammatory steroids, nonsteroidal anti-inflammatory, an immunizing suppressant (e.g. macrolides and derivatives), neural protective agents, growth factors (e.g. nerve, brain and/or tissue), anti-angiogenic agents, anti-proliferative agents, anticancer agents, anti comatous agents, enzymes, antioxidants, hormones, insuline, vitamins, antibiotics and antivirals.

[B0092] Biodendrimer is preferably used since this specific material has a high water content, and therefore there is a constant release of the beneficial substance over the desired time. Such a constant release eliminates or helps in the prevention of capsular opacification and inflammation. This method and device is helpful in recovery from surgical procedures, such as corneal or retinal surgery and any other suitable surgical procedures. Additionally, this method and device can be used as glaucoma filtering shunts or implants.

[B0093] The concentration of each of the beneficial substances is preferably between about 0.0001% and about 10% per volumes, but the concentration can be any suitable amount and does not necessarily need to be limited to those described herein.

[B0094] The substance is preferably injected or placed into the eye under the conjunctiva 154, but can be positioned in any suitable position in the eye or in any other place in the body. As a result, the biodendrimer forms part of a carrier system for controlled and/or extended release of a substance into the body. For example, the beneficial substance can release into the body or eye at continuously or substantially continuously for about one week to about two weeks. If the substance 150 is implanted or injected into the lens of the eye, the release time can be up to about one month to about two months or longer.

[B0095] Further, the drug, medicine, vitamin, nutrient or other therapeutic or beneficial substance can be encapsulated or otherwise treated to be more slowly released into or absorbed by the body (e.g., macroparticles, microspheres, nanoparticles or nanospheres); however, the substance is not necessarily treated to more slowly release into be absorbed by the body. For example, when encapsulated, the beneficial substance will release at a rate of about 1-3 months. Additionally, if the
substance 150 is inserted into the lens of the eye the release time may be extended up to about 3-6 months or longer.

[0096] An additional manner to prolong the release of the beneficial substance is to bind or chemically bond the biodendrimer molecules to the beneficial substance. This bonding is preferably done prior to injection or implantation into the body but can be done at any suitable time. Such bonding can prolong the release time to about 3-6 months or in some instances up to about one year. If the substance 150 is implanted or injected into the lens of the eye, bonding can increase the release time up to about 9 months to about 18 months or longer.

[0097] The biodendrimer can be loaded with a substance by dipping or soaking the biodendrimer in the substance or a solution including the substance, by mixing the biodendrimer with the substance, or by any other suitable manner; however, the biodendrimer is preferably loaded by injecting the substance into the biodendrimer.

[0098] When the loaded biodendrimer is positioned within the body, the beneficial substance gradually moves out of the biodendrimer and is released into the body. The period of release is preferably one month; however, the period of release can be any suitable period of time. Thus, a steady, localized release of a drug or other beneficial substance can be achieved, for example following eye surgery, throughout the initial healing period during which complications due to inflammation or infection are most likely.

[0099] The biodendrimer can be loaded before, during or after insertion into the body. Further, the biodendrimer can be reloaded via injection. Previous reloadable carrier systems required an incision to introduce the system into the body and to reload or replace the carrier. In contrast, the biodendrimer carrier system can be injected without an incision, and the biodendrimer carrier system can be reloaded via injection without an incision.

[00100] Fig. 24 shows a preferred process for introducing and reloading a biodendrimer carrier system into an eye. At step 2100, biodendrimer is injected via a syringe into the outer conjunctiva between the conjunctiva and the sclera. At step 2110, the biodendrimer is partly polymerized. Polymerization of biodendrimer can be photo initiated, chemically initiated, heat initiated, or initiated in any other suitable manner. At step 2120, before the biodendrimer is fully polymerized, the biodendrimer
is substantially flattened. Preferably, the biodendrimer was already loaded with the beneficial substance to be earned, however, if the biodendrimer was unloaded, or if additional loading is desired, at step 2130, the substance is injected into the biodendrimer via a syringe. At 2140, the substance is gradually released into the body. If reloading is desired at step 2150, the process repeats at step 2130.

[00101] It should be noted that the biodendrimer carrier system can be positioned anywhere in the body, as desired. Further, the high water contact provided by biodendrimer and the constant release of drug provided by loaded biodendrimer can help prevent opacification and/or inflammation and may make treatment with warm fluid 36 unnecessary when biodendrimer is used in an accommodating corrective lens as described below. Alternatively, the biodendrimer carrier system can be positioned at the site of any surgery, a tumor, a fracture, a strain, a tear, a joint, sub-dermal, intramuscular or any other suitable location, not limited to the eye.

[00102] It should also be noted that the biodendrimer of the biodendrimer carrier system can be biodegradable or permanent. If the biodendrimer is biodegradable, it can degrade over any suitable period of time, eliminating the need, if any, to remove the biodendrimer carrier system after it has served its purpose.

[00103] Fig. 25 illustrates a contact lens 160 that includes a mixture of a first material that includes biodendrimer and a second material that includes at least one other substance. It is noted that this lens does not necessarily need to be a contact lens and can be any refractive device desired. For example, it can be a subepithelial implant or onlay, an intrastromal implant or inlay or any other suitable device. If desired, the biodendrimer can be loaded as described above.

[00104] The second material preferably includes monomers and a polymerization initiator, such as a photosensitizer in the same or substantially similar manner as the method and system described above for each of the other embodiments. The second material does not necessarily need to include both monomers and a photosensitizer, and may include only monomers or a photosensitizer, or any other material that would enable the material to polymerize and or change shape and/or volume. Further, the second material can be biodendrimer or a mixture of biodendrimer and at least one other material.
[00105] Fig. 26 discloses another embodiment of the present invention, wherein contact lens 170 includes a first substance 172 and a second substance 174. It is noted that this lens does not necessarily need to be a contact lens and can be any refractive device desired. For example, it can be a subepithelial implant or onlay, an intrastromal implant or inlay or any other suitable device.

[00106] The first substance 172 has a first surface 176 and a second surface 178. The first surface faces in an anterior direction relative to the eye 10 and the second surface faces in a posterior direction to the 10. The second substance 174 is preferably attached or connected to the first substance overlying a portion of the first surface 176 can be attached or positioned on or relative to any surface or portion of the first substance desired.

[00107] The first substance is preferably biodendrimer and the second material includes at least one other substance. If desired, the biodendrimer can be loaded as described above.

[00108] The second material preferably includes monomers and a polymerization initiator, such a photosensitizer in the same or substantially similar manner as the method and system described above for each of the other embodiments. The second material does not necessarily need to include both monomers and a photosensitizer, and may include only monomers or a photosensitizer, or any other material that would enable the material to polymerize and or change shape and/or volume, as shown in Fig. 27. Further, the second material can be biodendrimer or a mixture of biodendrimer and at least one other material.

[00109] As shown in Fig. 27, portion 180 of second substance 174 is adapted to swell to change or alter the refractive properties of the lens 170 when exposed for light from laser 181. In this specific example, the outer peripheral portion of substance 174 is altered such that it swells and thereby decreases the curvature of the lens 170. However, it is noted that any portion of the second substance can be exposed to laser light (or any other suitable energy) to alter the refractive properties of lens 170 in any manner desired or to correct any refractive error present. For example, the lens can correct hyperopia, myopia, astigmatism, presbyopia or any other refractive error.

[00110] As shown in Fig. 28, first surface 176 or first substance 172 can have an aperture or blind opening 182 therein. Preferably opening 182 has a bottom surface
184 and side wall 186. Additionally opening 182 is substantially cylindrical and is positioned substantially in the center portion of first surface 176. However, opening 182 can have any configuration and positioning suitable.

[00111] Second substance 174 is preferably positioned within opening 182 and fits with the opening such that it lies immediately adjacent, abutting or in frictional contact with bottom surface 184 and wall 186. However, it is noted that substance 174 can be positioned within opening 182 in any suitable manner.

[00112] It is noted that each embodiment described herein can have its refractive properties altered via laser ablation. For example, any substance or material containing biodendrimer, silicon, or any other material or substance or any combination described herein can be exposed to a suitable laser (e.g. an excimer laser or a short pulse laser) to ablate any portion thereof, thus altering the refractive properties of the lens, implant or other device described herein.

[00113] Additionally, the biodendrimer carrier or substance 150 or any of the herein described implants, onlays, inlays or lenses can include a beneficial substance, such as a diagnostic agent. For example, the beneficial substance can change color based on the amount of glucose in the eye and/or body.

[00114] It should be understood that various changes and modifications to the presently preferred embodiments described herein will be apparent to those skilled in the art. Such changes and modifications can be made without departing from the spirit and scope of the present invention and without diminishing its intended advantages. It is therefore intended that such changes and modifications be covered by the appended claims.
The invention is claimed as follows:

1. A method of introducing a beneficial substance into the body comprising the steps of:
   loading biodendrimer with the beneficial substance; and
   positioning the biodendrimer relative to the body, such that the beneficial substance can be absorbed by the body.

2. The method of Claim 1, wherein the biodendrimer is loaded before the biodendrimer is injected.

3. The method of Claim 1, wherein the biodendrimer is loaded after the biodendrimer is injected.

4. The method of Claim 1, further comprising the step of:
   reloading the biodendrimer by injecting more of the beneficial substance into the biodendrimer after the steps of loading and injecting.

5. The method of claim 1, wherein
   the beneficial substance is encapsulated in microspheres.

6. The method of claim 1, wherein
   said beneficial substance includes at least one of the following anti-inflammatory agents, immunizing suppressants, neural protective agents, growth factors, anti-angiogenic agents, anti-proliferative agents, anticancer agents, anti-comatous agents, enzymes, antioxidants, hormones, insulin, vitamins, antibiotics and antivirals.

7. The method of claim 1, wherein
   the step of positioning the biodendrimer relative to the body includes injecting the biodendrimer beneath the conjunctiva of an eye.
8. The method of claim 1, wherein
the step of positioning the biodendrimer relative to the body includes placing
the biodendrimer into a lens and inserting the lens into the eye.

9. A method of claim 8, wherein
the lens is selected from the group consisting of an intrastromal inlay, a
subepithelial onlay and an intraocular lens.

10. The method of claim 1, wherein
the step of positioning the biodendrimer relative to the body includes placing
the biodendrimer into a lens and positioning the lens on an exterior surface of the
cornea.

11. The method of claim 1, wherein
the step of loading biodendrimer with the beneficial substance includes loading
the biodendrimer with the beneficial substance encapsulated in microparticles.

12. A device for introducing a beneficial substance into the body, comprising:
a first substance including biodendrimer;
a second substance that has properties beneficial to the body.

13. A device according to claim 12, wherein
said second substance is adapted to be injected into the first substance.

14. A device according to claim 12, wherein
said first substance is adapted to be inserted into the eye.

15. A device according to claim 12, wherein
said second beneficial substance includes at least one of the following anti¬
inflammatories, immunizing suppressants, neural protective agents, growth factors,
anti-angeogentic agents, anti-proliferative agents, anticancer agents, anti comatous
agents, enzymes, antioxidants, hormones, insuline, vitamins, antibiotics and antivirals.
16. A lens for altering the refractive properties of the eye, comprising:
   a first material including biodendrimer;
   a second material adapted to change the shape of the lens when exposed to an energy source.

17. A lens according to claim 16, wherein the lens is loaded with a beneficial substance.

18. A lens according to claim 16, wherein said lens is a contact lens.

19. A lens according to claim 18, wherein said first material has a first surface and a second surface, said first surface adapted to be positioned facing in an anterior direction of the eye and said second surface adapted to be positioned facing in a posterior direction of the eye; and said second material attached to said first surface of said first material.

20. A lens according to claim 19, wherein said first surface includes an opening a said second material is positioned within said opening.
START

2100 BIODENDRIMER IS INJECTED VIA A SYRINGE INTO THE OUTER CONJUNCTIVA BETWEEN THE CONJUNCTIVA AND THE SCLERA

2110 THE BIODENDRIMER IS PARTLY POLYMERIZED

2120 BEFORE THE BIODENDRIMER IS FULLY POLYMERIZED, THE BIODENDRIMER IS SUBSTANTIALLY FLATTENED

2130 THE SUBSTANCE IS INJECTED INTO THE BIODENDRIMER VIA A SYRINGE

2140 THE SUBSTANCE IS GRADUALLY RELEASED INTO THE BODY

2150 IS RELOADING DESIRED?

YES

NO

END

FIG. 24
INTERNATIONAL SEARCH REPORT

A. CLASSIFICATION OF SUBJECT MATTER

IPC: A61K 51/00 (2006.01); A61M 36/14 (2006.01)

USPC: 424/1.33, 423

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S.: 424/1.33, 423

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

EAST Brs search

C. DOCUMENTS CONSIDERED TO BE RELEVANT

<table>
<thead>
<tr>
<th>Category</th>
<th>Citation of document, with indication, where appropriate, of the relevant passages</th>
<th>Relevant to claim No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>X</td>
<td>US 5,527,524 A (TOMALIA et al.) 18 June 1996 (18.06.1996), examples, abstract.</td>
<td>1, 2, 6, 12, 13, 15</td>
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Further documents are listed in the continuation of Box C. See patent family annex.

Date of the actual completion of the international search

24 June 2006 (24.06.2006)

Name and mailing address of the ISA/US

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03 JUL 2006

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