tattoo on the body; and maintaining contact with skin or hair for an extended period of time, such as with moisturizing or regenerative agents overnight. The substance could also serve for offering an extended efficacy of insect repellents, allowing limited need for re-dosing and thereby reducing the overall exposure to the repellent. Alternatively, the substance could serve as an inert protective layer to be applied on the skin before using a mosquito or other insect repellent, maintaining the efficacy of the repellent while protecting the skin or any other mucosa from the toxicity or other effects of the repellant.

SUMMARY

The present disclosure relates to compositions and methods for separating the different aspects of the uterine cavity, or other body cavities or tissues, typically for a controlled period of time, as for example 2-4 weeks, after surgery and for preventing post-surgical scarring. In the uterus, this ultimately prevents the classical complications, including uterine synechiae, and the ensuing infertility. Other than the uterus, this prevents similar complications inherent to the particular site of surgery.

In one aspect, there is provided a phase shifting formulation, comprising a suitable gel-forming polymer in a composition that is placed on a post-surgical tissue surface and keeps local tissues separated while allowing healing, wherein the gel-forming polymer is capable of undergoing a change in viscosity or liquefaction or otherwise lose viscosity upon exposure to a trigger, the trigger being selected from a change in salt concentrations, an exothermic or endothermic reaction, a direct change in temperature, a change in pH, a physical disruption, a displacement from the tissue, or a passage of time.

In another aspect, there is provided a phase shifting formulation of the present invention for use in preventing post-surgical scarring and/or other adhesions.

In another aspect, there is provided a phase shifting formulation of the present invention for use in minimizing or preventing infection or inflammation, or for use during a cosmetic procedure, or for use in protecting a patient's burns, or for use in protecting a wound from infection or from further damage pending medical attention, or for use in maintaining a skin graft in place.

In yet another aspect, there is provided a phase shifting formulation of the present invention for use in facilitating diagnosis of damage or developing lesions in or near a joint of the patient.

The composition of the present disclosure is to be applied after surgery, such as uterine surgery. The composition will consist as a gel or a semi-solid substance that will keep the uterine wall separated for a controlled period of time set to match the time needed so that the normal lining develops while scarring is prevented after surgery. The composition uses phase-shifting properties adapted for the specific needs encountered after the particular surgery. After uterine surgery, for example, about 2-20 ml of the composition will be applied at the end of the surgical procedures (quantity depending on uterine size and the nature of surgery performed), using a catheter. The composition will retain its ability to keep the uterine tissues separated,

locally effective medications, anti-inflammatory, anti-infectives, or diagnostic agents, for extended periods, which could not be done before.

During scar prevention by the composition, ultrasound examination can allow visualization to confirm that the needed slight uterine distension is maintained. If needed, a new administration of the composition could be used to extend the duration of treatment and/or to further maintain wall separation.

Prior to injecting the composition in the uterine cavity, various therapeutic products can be applied locally in the uterine cavity such as anti-inflammatory and healing promoting substances, to further reduce the risk of scarring. In some examples, the composition further includes such substances within its formulation. The substances that can be used locally before applying, or included within, the composition for maintaining the desired separation between the opposing aspects of the uterine cavity include, but are not limited to: corticosteroids, estrogenic hormones, progesteronic hormones, NSAID preparations, protectorants, various anti-oxidants and/or all active preparations that are commonly found in balms, creams, gels, lotions and ointments used in other healing and/or as topical anti-inflammatory preparations. Possible substances further include, but are not limited to, aspirin, salicylic acid derivatives, zinc oxide, vitamins A, C or E (and derivatives), tissue growth factors, stem cell derived tissue grafts, and emollients, all used in concentration ranges commonly used in practice. The composition would help maintaining contact between such substances and the endometrial mucosa. Endometrial cells with stem-cell like pluri-potent properties could also be placed over the surfaces left raw by surgery. Endometrial cells from the basal layer display pluri-potent properties that make them true stem cells. Such cells collected from a healthy area of the endometrium could be replaced in thin layer over the raw surfaces left after uterine surgery.

This process could take place directly with cells collected and replaced elsewhere during the same procedure. Alternatively, endometrial cells from healthy areas could be obtained before the scheduled uterine surgery and made to multiply in vitro in order to obtain a sufficient amount for covering the raw surfaces at the end of the uterine surgery. Such cells could either be simply layered over the desired area where regeneration of a normal endometrium is desired or held in some sort of mesh designed to play a holding role or scaffold. The latter can be made of persistent or resorbing material.

But cells that would be simply layered on the damaged endometrial surface would be washed away before having the chance of regenerating a proper uterine lining. On the contrary, the composition, applied just after the cells are layered, would help keep them in place for the desired duration. By providing a practical way of holding cells in place, the composition could therefore make cell therapy possible for the regeneration of damaged endometrium. In that, the composition could be crucial for preserving or restoring a functional lining of the uterine cavity. Ultimately therefore, the composition could markedly change the prospect of pregnancy after uterine surgery.

The skills and knowledge base to produce effective anti-inflammatory and cell therapy formulations is standard among those skilled in the art. In particular, the preparations susceptible of helping the healing process of the endometrium after surgery of the endometrium have known application to mucosal and epithelial surfaces. Currently however the use of such formulations and cell therapy is simply impractical. The invention, which makes these options possible, allows for the timing necessary to have these formulations perform as needed to offer the desired results.

CLAIMS

What is claimed is:

1. A phase shifting formulation, comprising a suitable gel-forming polymer in a composition that is placed on a post-surgical tissue surface and keeps local tissues separated while allowing healing, wherein the gel-forming polymer is capable of undergoing a change in viscosity or liquefaction or otherwise lose viscosity upon exposure to a trigger, the trigger being selected from a change in salt concentrations, an exothermic or endothermic reaction, a direct change in temperature, a change in pH, a physical disruption, a displacement from the tissue, or a passage of time.

2. The phase shifting formulation of claim 1, wherein the gel-forming polymer is selected from a cellulose, a carbomer, gelatin, agar, pectin, a starch, high molecular weight polyethylene glycol, a poloxamer, and a colloidal clay.

3. The phase shifting formulation of claim 1 or 2, wherein the formulation further comprises a treating agent or tissue regeneration stimulating agent to promote healing and/or regeneration.

4. The phase shifting formulation of any of the preceding claims, wherein the treating agent or tissue regeneration stimulating agent is selected from endometrial cells with stem-cell like pluri-potent properties; a glycoprotein; a protein; a peptide; a sex hormone; an anti-hormone; a selective estrogen and progestin receptor modulator; a nitrate; a beta-agonist; a beta-antagonist; an opioid; an opioid-antagonist; an antidepressant; a HMG CoA reductase inhibitor; an antihistamine; an ACE inhibitor; a prostaglandin; a semisynthetic or synthetic derivative of a natural prostaglandin; a non-steroidal anti-inflammatory drug (NSAID); an anti-infective; an anesthetic; an immune system modifier; a muscarinic agonist; a muscarinic antagonist; an anti-neoplastic agent; vitamin K; ondansetron; levocarnitine; an anti-fungal; carbamide peroxide; a dopamine antagonist; a bisphosphonate; nicotine; an anti-virals agent; an anti-diabetagenic; insulin; an anti-Parkinson agent; a low molecular weight heparin; an antimicrobial; an anti-cancer agent; and an anti-infective compound;
wherein the treating agent or tissue regeneration stimulating agent is optionally selected from follicle-stimulating hormone (FSH), luteinizing hormone (LH), human chorionic

gonadotropin (HCG), thyroid-stimulating hormone (TSH), GnRH (agonist and antagonist), desmopressin, oxytocin analogs, insulin analogs, TRH analogs, somatostatin analogs, tissue plaminogen activator (TPA), growth hormone releasing hormone (GHRH), corticotropin-releasing hormone analogs (CRH analogs), estradiol, testosterone, progesterone, tamoxifen, mifepristone, raloxifene, nitroglycerin, isosorbide, erythrityl tetranitrate, pentaerythritol tetranitrate, terbutaline, albuterol, pirbuterol, bitolterol, ritodrine, propranolol, metoprolol, nadolol, atenolol, timolol, esmolol, pindolol, acebutolol, labetalol, morphine, hydromorphone, oxymorphone, codeine, hydrocodone, oxycodone, levorphanol, levallorphan, buprenorphine, fentanyl, nalbuphine, butorphanol, pentazocine, naloxone, nalmefene, amitriptyline, amoxapine, desipramine, doxepin, imipramine, maprotilen, nortriptyline, protripyline, trimipramine, fluoxetine, trazodone, lovastatin, mevastatin, simvastatin, pravastatin, atorvastatin, loratadine, chlorpheniramine maleate, brompheniramine maleate, diphenhydramine, dimenhydrinate, carbinoxamine, promethazine, tripelannamine, captopril, enalapril, Lisinopril, prostaglandin E_2 ("PGE_2"), PGE_1, PGA_1, PGB_1, $PGF_{1\alpha}$, 19-hydroxy-PGA_1, 19-hydroxy-PGB_1, PGA_2, PGB_2, 19-hydroxy-PGA_2, 19-hydroxy-PGB_2, PGE_3, $PGF_{3\alpha}$, mioprostol, carboprost trometharnine, dinoprost tromethamine, dinoprostone, lipoprost, gemeprost, metenoprost, sulprostone,tiaprost; diclofenac, etodolac, fenoprofen, lurbiprofen, ibuprofen, indomethacin, ketoprofen, ketorolac, meclofenamate, fenamic acid, meloxicam, nabumetone, naproxin, oxaprozin, piroxicam, sulindac, tolmetin, lidocaine, cocaine, chloroprocaine, tetracaine, prilocaine, mepivacaine, buipivacaine, levobupivacaine, articaine, ropivacaine, phenol, benzocaine, pramoxine, dyclonine, etidocaine, procaine, proparacaine, dibucaine, pramoxine, imiquimod, bethanecol oxybutinyn, melphalan, fluorouracil, a vinca alkaloid, bleomycin, cisplatin, vitamin K, ondansetron, levocarnitine, carbamide peroxide, bromocriptine, a bisphosphonate, nicotine, acyclovir, metformin, octreatide, desmopressin, GNRH, insulin, levodopa, metronidazole; a heavy metal, a salt, and a radio-active substance.

5. A phase shifting formulation of any of claims 1 to 4 for use in preventing post-surgical scarring and/or other adhesions.

6. The phase shifting formulation of claim 5, wherein the phase shifting formulation is to be applied to a patient's uterus, to a patient's fallopian tubes, to a patient's colon, to a patient's urethra, to a patient's bladder or to a patient's skin graft.

7. The phase shifting formulation of claim 5 or 6, wherein the phase shifting formulation is to be applied to the uterine cavity after surgery that involves the uterine cavity.

8. The phase shifting formulation of any of claims 5 to 7, wherein the phase shifting formulation is to be removed by a trigger that causes the formulation to lose its integrity to facilitate removal from the body cavity or tissue surface.

9. The phase shifting formulation of claim 6, wherein the phase shifting formulation is to be applied to a patient's uterus after surgery that involves the uterine cavity or is to be applied to a patient's skin graft, and wherein the phase shifting formulation is to be removed by a trigger 10-20 days after surgery.

10. The phase shifting formulation of any of claims 5 to 9, wherein the post-surgical scarring and/or other adhesions are in the uterus after surgery, wherein:

the phase shifting formulation is to be administered to the uterine cavity so as to maintain space between the local tissues and avoid scarring or other adhesions;

the phase shifting formulation is allowed to remain substantially in place in the uterine cavity for a period of time sufficient to allow healing; and

a trigger is to be used to liquefy or remove the gel or semi-solid substance from the uterine cavity atraumatically.11. The phase shifting formulation of any of claims 5 to 10, wherein the phase shifting formulation is to be injected into the uterus after a therapeutic product has been applied locally in the uterine cavity.

12. The phase shifting formulation of any of claims 5 to 11, wherein the composition maintains an initial viscosity or consistency for a time sufficient to maintain the subject body tissue free from contact with other tissue or objects, wherein the composition is to be implaced to coat or cover the site of the procedure that requires healing; the composition is then allowed to, after a suitable amount of time, reduce in viscosity or consistency over the relatively short period of time; the reduced viscosity or reduced consistency composition is to be removed or allowed to expulse from the body tissue; and a fresh amount of the composition is to be implaced repeatedly if and as needed until the risk of scarring or adhesions has decreased significantly.

13. A phase shifting formulation of any of claims 1 to 4 for use in minimizing or preventing infection or inflammation, or for use during a cosmetic procedure, or for use in protecting a patient's burns, or for use in protecting a wound from infection or from further damage pending medical attention, or for use in maintaining a skin graft in place.

14. A phase shifting formulation of any of claims 1 to 4 for use in facilitating diagnosis of damage or developing lesions in or near a joint of the patient.

15. The phase shifting formulation of claim 13 or 14, wherein the use optionally includes placing additional treating agents either separately before the formulation is to be applied, or within the viscosity-shifting composition.