[0007] European patent No. 1 080 698, filed in 1993, discloses an injectable soft tissue augmentation material comprising finely divided ceramic particles (e.g., CaHA) and covers *inter alia*, Radiesse®. In addition, WO 2014/056723 describes a viscoelastic gel comprising crosslinked HA at a concentration of between 1% and 4% (w/v) and hydroxyapatite particles at a concentration of between 10% and 70% (w/v).

OBJECT OF THE INVENTION

[0008] In view of the above, the object of the present invention is to provide a long-lasting dermal filler composition having improved rheological properties while at the same time being easily injectable.

SUMMARY

[0009] The above object is solved by the provision of an injectable dermal filler composition in the form of a gel that makes use of carboxymethyl cellulose as a lubricant. This new type of dermal filler offers good longevity, is easily injectable and has improved rheological properties (i.e. G Prime (G') and dynamic viscosity) resulting in an excellent ability to create volume. In one aspect, the present disclosure refers to an injectable dermal filler composition in the form of a gel, comprising crosslinked hyaluronic acid and carboxymethyl cellulose as a lubricant/lubricant phase, wherein the carboxymethyl cellulose is present at a concentration of 1.0% to 25.0% volume/volume, wherein the crosslinked hyaluronic acid is crosslinked with 1,4-butanediol diglycidyl ether.

[0010] In one example, there is disclosed an injectable dermal filler composition in the form of a gel, comprising crosslinked (e.g., BDDE crosslinked) hyaluronic acid (HA) and carboxymethyl cellulose (CMC).

[0011] The crosslinked HA is usually present in a concentration of 0.1% to 4.0% weight/volume (e.g., 0.5% to 4.0% or 1.0% to 4.0% weight/volume) and provides a crosslinked matrix, whereas the CMC is usually present in a concentration of 1.0% to 25% volume/volume and is added as a lubricant/lubricant phase. In one example, the

injectable dermal filler composition further comprises resorbable biocompatible microparticles, in particular calcium hydroxyapatite microparticles.

[0012] In another aspect, the present disclosure refers to a kit comprising the injectable dermal filler composition according to the first aspect of the invention.

[0013] In yet another aspect, the present disclosure refers to a method for preparing an injectable dermal filler composition as disclosed herein, comprising the following steps:

(a) providing a crosslinked hyaluronic acid gel,
(b) providing a carboxymethyl cellulose gel,
(c) mixing the crosslinked hyaluronic acid gel and the carboxymethyl cellulose gel.

[0014] In one example, there is disclosed the use of an injectable dermal filler composition or of the kit as disclosed herein for cosmetic applications such as treatment of facial lines. In one aspect, the present disclosure refers to use of an injectable dermal filler composition or a kit as disclosed herein for cosmetic applications, including cosmetic treatment of wrinkles and lines of the skin, glabellar lines, nasolabial folds, chin folds, marionette lines, jawlines, buccal commissures, perioral wrinkles, crow's feet, cutaneous depressions, scars, temples, subdermal support of the brows, malar and buccal fat pads, tear troughs, nose, lips, cheeks, chin, perioral region, infraorbital region, and facial asymmetries

[0015] In another example, there is disclosed an injectable dermal filler composition according to the first aspect of the invention or of a kit according to the second aspect of the invention for use in therapy, in particular for use in treating stress urinary incontinence, vesico-ureteral reflux, vocal fold insufficiency, and vocal fold medialization.

[0016] In yet another example, there is disclosed a method for replacing or filling of a biological tissue or increasing the volume of a biological tissue, comprising

CLAIMS

1. An injectable dermal filler composition in the form of a gel, comprising crosslinked hyaluronic acid and carboxymethyl cellulose as a lubricant/lubricant phase, wherein the carboxymethyl cellulose is present at a concentration of 1.0% to 25.0% volume/volume, wherein the crosslinked hyaluronic acid is crosslinked with 1,4-butanediol diglycidyl ether.

2. The injectable dermal filler composition of claim 1, wherein the crosslinked hyaluronic acid is present at a concentration of 1.0% to 4.0% weight/volume.

3. The injectable dermal filler composition of claim 1 or 2, wherein the crosslinked hyaluronic acid has a degree of modification, expressed as the ratio of the sum of mono- and double-linked BDDE-crosslinkers to the sum of hyaluronic acid disaccharide units, of 0.5% to 25%.

4. The injectable dermal filler composition of any one of claims 1 to 3, wherein the composition further comprises resorbable biocompatible microparticles in a concentration of 1% to 50% volume/volume.

5. The injectable dermal filler composition of claim 4, wherein the resorbable biocompatible microparticles consist of calcium phosphate-based materials, alumina-based materials, a biodegradable natural polysaccharide or a derivate thereof, or a biodegradable polyester, polyorthoester or polyanhydride synthetic polymer, wherein the calcium phosphate-based materials include calcium hydroxyapatite, calcium fluoroapatite, calcium chloroapatite, calcium carbonate apatite, tetracalcium phosphate, calcium pyrophosphate, tricalcium phosphate, and octacalcium phosphate.

6. The injectable dermal filler composition of any one of claims 1 to 5, further comprising one or more compounds selected from the group consisting of anesthetics, polyols, vitamins, amino acids, metals, antioxidants, and mineral salts.

7. The injectable dermal filler composition of any one of claims 1 to 6, wherein the composition comprises a polyol and/or an anesthetic.

8. The injectable dermal filler composition of any one of claims 1 to 7, wherein the composition has one or more of the following properties:

   (i) an elastic modulus G' at a frequency (f) of 0.4 Hz and 25°C of 100 Pa to 4000 Pa;

   (ii) a viscosity at a frequency of 0.4 Hz and 25°C of 20 Pa·s to 1000 Pa·s; and

   (iii) a tan delta (G''/G') at a frequency of 0.4 Hz and 25°C of 0.25 to 0.6.

9. A kit comprising the injectable dermal filler composition according to any one of claims 1 to 8.

10. A method for preparing an injectable dermal filler composition according to any one of claims 1 to 8, comprising the following steps:

   (a) providing a crosslinked hyaluronic acid gel,
   (b) providing a carboxymethyl cellulose gel,
   (c) mixing the crosslinked hyaluronic acid gel and the carboxymethyl cellulose gel.

11. Use of an injectable dermal filler composition according to any one of claims 1 to 8 or a kit according to claim 9 for cosmetic applications, including cosmetic treatment of wrinkles and lines of the skin, glabellar lines, nasolabial folds, chin folds, marionette lines, jawlines, buccal commissures, perioral wrinkles, crow's feet, cutaneous depressions, scars, temples, subdermal support of the brows,

malar and buccal fat pads, tear troughs, nose, lips, cheeks, chin, perioral region, infraorbital region, and facial asymmetries.

12. An injectable dermal filler composition according to any one of claims 1 to 8 or a kit according to claim 9 for use in therapy.

13. An injectable dermal filler composition according to any one of claims 1 to 8 or a kit according to claim 9 for use in treating stress urinary incontinence, vesico-ureteral reflux, vocal fold insufficiency, and vocal fold medialization.