

example, lidocaine, when subjected to sterilization techniques such as autoclaving, and/or when stored for long periods at ambient temperature. Methods for preparing such HA-based compositions are also provided as well as products made by such methods.

5 [0014a] In one aspect, there is provided a method of preparing a soft tissue filler composition, the method comprising the steps of:

providing a hyaluronic acid (HA) component crosslinked with at least one crosslinking agent selected from the group consisting of 1,4-butanediol diglycidyl ether (BDDE), 1,4-bis(2,3-epoxypropoxy)butane, 1,4-bisglycidyloxybutane, 1,2-bis(2,3-epoxypropoxy)ethylene and 1-(2,3-epoxypropyl)-2,3-epoxycyclohexane, or combinations thereof;

dialyzing the hyaluronic acid (HA) component against a phosphate buffer so that the pH is 7.2;

15 adjusting the pH of said hyaluronic acid (HA) component from 7.2 to an adjusted pH of 7.5 to 8; and

adding lidocaine HCl to said hyaluronic acid (HA) component at said adjusted pH of 7.5 to 8 to obtain said soft tissue filler composition.

[0014b] In one aspect, there is provided a method of preparing a cohesive hyaluronic acid (HA)-based filler composition, the method comprising the steps of:

20 providing dry uncrosslinked sodium hyaluronate (NaHA) material and hydrating said dry uncrosslinked sodium hyaluronate (NaHA) material in an alkaline solution to obtain an alkaline, uncrosslinked sodium hyaluronate (NaHA) gel;

crosslinking said uncrosslinked sodium hyaluronate (NaHA) gel with 1,4-butanediol diglycidyl ether to form a crosslinked alkaline hyaluronic acid composition with a pH above 7.5;

25 adding a solution containing lidocaine HCl to said hyaluronic acid (HA) component having said adjusted pH above 7.5 to obtain said hyaluronic acid (HA)-based filler composition;

homogenizing said hyaluronic acid (HA)-based filler composition thereby forming a homogenized hyaluronic acid (HA)-based filler composition;

30 and sterilizing said homogenized hyaluronic acid (HA)-based filler composition thereby forming said cohesive hyaluronic acid (HA)-based filler composition.

wherein said cohesive hyaluronic acid (HA)-based filler composition comprises 5% to 95% of a hyaluronic acid (HA) component having a molecular weight of greater than 1.0 MDa with the balance of the hyaluronic acid (HA) material being a hyaluronic acid (HA) component having a molecular weight of less than 1.0 MDa.

[0014c] In one aspect, there is provided a method of adding lidocaine to a crosslinked hyaluronic acid (HA) composition comprising:

providing a 1,4-butanediol diglycidyl ether (BDDE) crosslinked hyaluronic acid (HA) composition having a pH 7.2 or lower;

increasing the pH of the composition to at least about 7.5;

adding lidocaine to the composition; and

sterilizing the composition by autoclaving the composition.

[0015] Described herein are soft tissue filler compositions, the compositions generally comprising: a hyaluronic acid component crosslinked with a crosslinking agent selected from the group consisting of 1,4-butanediol diglycidyl ether (BDDE), 1,4-bis(2,3-epoxypropoxy)butane, 1,4-bisglycidyl ether, 1,2-bis(2,3-epoxypropoxy)ethylene and 1-(2,3-epoxypropyl)-2,3-epoxycyclohexane, and 1,4-butanediol diglycidyl ether; and at least one anesthetic agent combined with the crosslinked HA component.

[0016] In yet another embodiment, the at least one anesthetic agent is lidocaine. In a further embodiment, the amount of the anesthetic agent is present at a concentration between about 0.1% and about 5.0% by weight of the composition. In still another embodiment, the anesthetic agent is present at a concentration between about 0.2% and about 1.0% by weight of the composition. In one embodiment, the anesthetic agent is lidocaine and is present at a concentration of about 0.3% by weight of the composition.

[0017] In still another embodiment, the soft tissue filler composition has an extrusion force of between about 10 N and about 13 N, for example, at a rate of about 12.5 mm/minute. In yet another embodiment, the composition has a viscosity of between about 5 Pa*s and about 450 Pa*s, for example, when measured at about 5 Hz.

[0018] In one embodiment, the HA component is a gel, for example, a cohesive, hydrated gel. In one embodiment, the HA component is a crosslinked HA gel having no greater than about 1% to about 10% free HA. For purposes of this disclosure, free HA includes truly free HA as well as
5 lightly crosslinked HA chains and fragments, all in soluble form in water.