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### (54) CROSSLINKED HYALURONIC ACID COMPOSITIONS FOR TISSUE AUGMENTATION

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- 514/2; 514/44; 424/130.1; 536/53

### ABSTRACT (57)

A hyaluronic acid (HA) composition includes crosslinked, water-insoluble, hydrated HA gel particles. The HA includes crosslinks represented by the following structural formula:

HA-U-R2-U-HA

The variables are defined herein.

A method of augmenting tissue in a subject includes inserting a needle into a subject at a location in the subject that is in need of tissue augmentation, wherein the needle is coupled to a syringe loaded with the HA composition, and applying force to the syringe, to deliver the HA composition into the subject.

A method of preparing the HA composition, includes forming water-insoluble, dehydrated crosslinked HA particles, separating the water-insoluble, dehydrated particles by average diameter, selecting a subset of particles by average diameter, and hydrating the subset of dehydrated particles with a physiologically compatible aqueous solution.

Another method of preparing the crosslinked HA composition includes crosslinking a precursor of the crosslinked HA with a biscarbodiimide in the presence of a pH buffer and dehydrating the crosslinked HA.

Also included is a method of augmenting tissue in a subject that is in need of tissue augmentation.

A method of stabilizing crosslinked HA includes hydrating water-insoluble, dehydrated crosslinked HA with a physiologically compatible aqueous solution that includes a local anesthetic, wherein the value of storage modulus G' for the stabilized composition is at least about 110% of the value of G' for a non-stabilized composition,.

Also included is the stabilized HA composition.

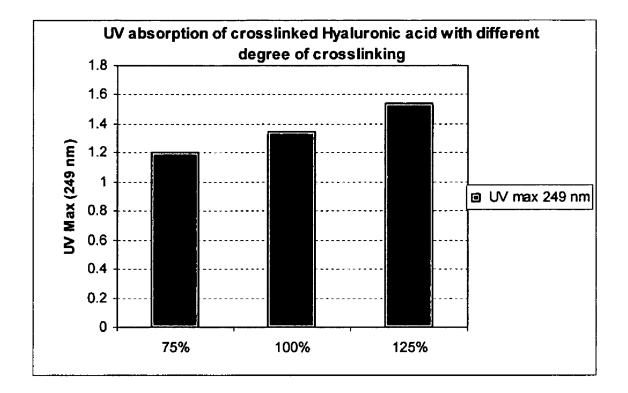


FIG. 1

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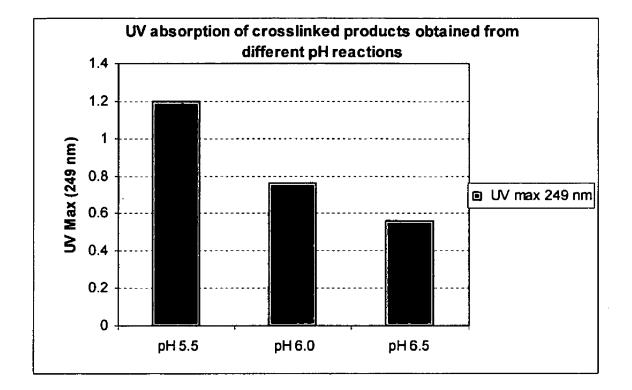


FIG. 2

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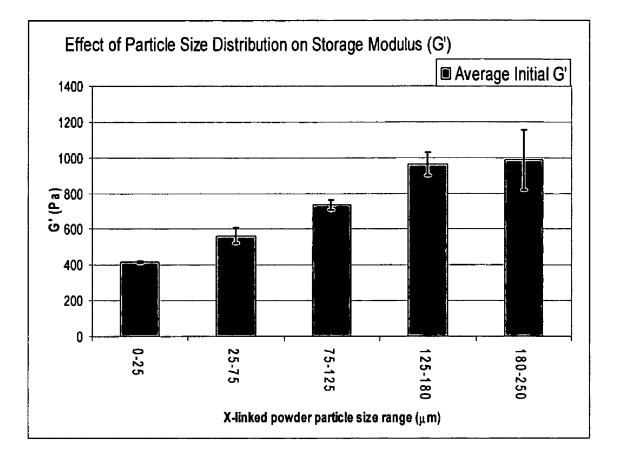
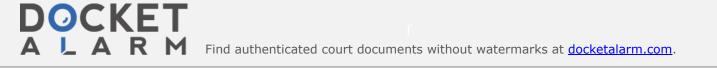


FIG. 3



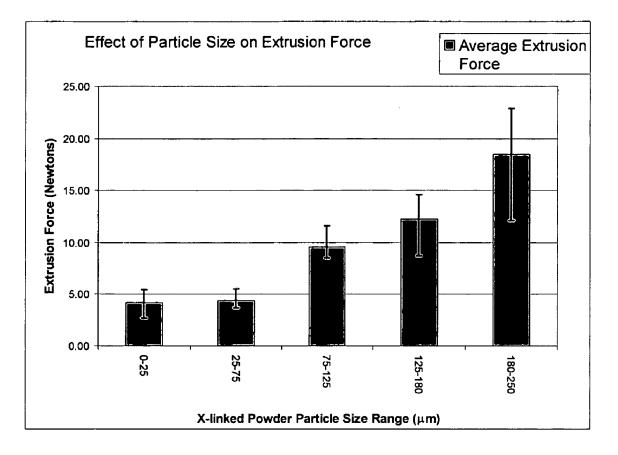


FIG. 4

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