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(54) **STABLE SILK PROTEIN FRAGMENT COMPOSITIONS**

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(58) **Field of Classification Search**

None

See application file for complete search history.

(56) **References Cited**

U.S. PATENT DOCUMENTS

6,902,932	B2	6/2005	Altman et al.
7,632,873	B2	12/2009	Mougin
7,635,755	B2	12/2009	Kaplan et al.
7,674,882	B2	3/2010	Kaplan et al.
7,727,542	B2	6/2010	DiBenedetto et al.
8,071,722	B2	12/2011	Kaplan et al.
8,187,616	B2	5/2012	Wang et al.

(Continued)

FOREIGN PATENT DOCUMENTS

WO	2012/145739	10/2012
WO	2014/011644	1/2014
WO	2014/145002	9/2014

OTHER PUBLICATIONS

Wang, Q., et al. Biomacromolecules (2012), 14; pp. 285-289.*

Gilbert et al., "Dispersity in Polymer Science", Pure Appl. Chem., 2009, 81(2), pp. 351-353.

Cetinkaya et al., "Silk Fiber Mechanics from Multiscale Force Distribution Analysis", Biophysical Journal, Mar. 2011, 100(5), pp. 1298-1305.

(Continued)

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(57) **ABSTRACT**

A composition is disclosed that includes pure silk fibroin-based protein fragments that are substantially devoid of sericin, wherein the composition has an average weight average molecular weight ranging from about 17 kDa to about 38 kDa, wherein the composition has a polydispersity of between about 1.5 and about 3.0, wherein the composition is substantially homogeneous, wherein the composition between 0 ppm to about 500 ppm of inorganic residuals, and wherein the composition includes between 0 ppm to about 500 ppm of organic residuals.

22 Claims, 105 Drawing Sheets