[0005] Incumbent to cell culture is adequate oxygenation and supply of nutrients to the cells. An associated challenge includes stirring of the microcarriers to provide the required oxygen and nutrients without introducing hydrodynamic stresses sufficient to damage the growing cells. Conventionally the stirring is done using impellers.

[0006] A further challenge involves separating the microcarriers from the cells or conditioned media. Enzymatic treatment may be used to harvest adhesive cells, for example, though the addition of enzymes can damage the cells. Proteolytic enzymes, for example, may non-selectively clear cell surface receptors.

[0007] Effective cell recovery from microcarriers often requires the use of concentrated enzymes, extended treatment times, and continuous centrifugation / filtration cycles, which can negatively affect cell health and recovery yield. Further, there are questions about possible by-products from microcarrier digestion and the effect such by-products may have on cell health and recovery yield.

[0008] In view of the foregoing, it would be advantageous to provide cell growth surfaces including microcarriers having with defined digestion by-products, as well as methods of effectively culturing and harvesting cells from growth surfaces while controlling digestion by-products.

~~BRIEF~~ SUMMARY

[0009] In ~~accordance with embodiments of~~ the present disclosure, a cell culture article comprises a cell culture article is ~~providing~~provided. The article includes a substrate having a polygalacturonic acid compound crosslinked with a divalent cation, the polygalacturonic acid compound selected from at least one of: pectic acid; partially esterified pectic acid, partially amidated pectic acid and salts thereof. The substrate is digestible by digestion reagents into components comprising of galacturonic acid monomers and the divalent cation.

[0009a] In one aspect, the present disclosure refers to a cell culture article, comprising: a substrate comprising a polygalacturonic acid compound crosslinked with a divalent cation, the polygalacturonic acid compound selected from at least one of: pectic acid; partially esterified pectic acid, partially amidated pectic acid and salts thereof; wherein the substrate is digestible by

digestion reagents into components comprising of galacturonic acid monomers and the divalent cation.

[0010] In ~~other embodiments~~the present disclosure, a method of harvesting cultured cells from a dissolvable substrate is provided. The method include separating the cultured cells from the substrate by digesting the substrate via exposure of the substrate to (i) a chelating agent, (ii) an enzyme, or (iii) a chelating agent and an enzyme, the separating resulting in a harvest solution; and

performing a series of wash and/or centrifugation cycles of components of a harvest solution following the separating. The substrate comprising a polygalacturonic acid compound selected from at least one of: pectic acid; partially esterified pectic acid, partially amidated pectic acid and salts thereof, and an adhesion polymer on the surface of the polygalacturonic acid compound.

[0010a]In another aspect, the present disclosure refers to a method of harvesting cultured cells from a dissolvable substrate, the method comprising: separating the cultured cells from the substrate by digesting the substrate via exposure of the substrate to (i) a chelating agent, (ii) an enzyme, or (iii) a chelating agent and an enzyme, the separating resulting in a harvest solution; and performing a series of wash and/or centrifugation cycles of components of a harvest solution following the separating, wherein the substrate comprising a polygalacturonic acid compound selected from at least one of: pectic acid; partially esterified pectic acid, partially amidated pectic acid and salts thereof, and an adhesion polymer on the surface of the polygalacturonic acid compound.

[0011] Additional features and advantages of the subject matter of the present disclosure will be set forth in the detailed description which follows, and in part will be readily apparent to those skilled in the art from that description or recognized by practicing the subject matter of the present disclosure as described herein, including the detailed description which follows, the claims, as well as the appended drawings.

[0012] It is to be understood that both the foregoing general description and the following detailed description present embodiments of the subject matter of the present disclosure, and are intended to provide an overview or framework for understanding the nature and character of the subject matter of the present disclosure as it is claimed. The accompanying drawings are included to provide a further understanding of the subject matter of the present disclosure, and are incorporated into and constitute a part of this specification. The drawings illustrate various embodiments of the subject matter of the present disclosure and together with the description serve to explain the principles and operations of the subject matter of the present disclosure. Additionally, the drawings and descriptions are meant to be merely illustrative, and are not intended to limit the scope of the claims in any manner.

BRIEF DESCRIPTION OF THE DRAWINGS

[0013] The following detailed description of specific embodiments of the present disclosure can be best understood when read in conjunction with the following drawings, where like structure is indicated with like reference numerals and in which:

[0014] Fig. 1 is a phase contrast image showing hMSC cells on externally crosslinked PGA microcarriers according to an embodiment;

[0015] Fig. 2 is a phase contrast image showing hMSC cells on externally crosslinked PGA microcarriers according to a further embodiment;