crosslinked with a divalent cation. The divalent cation concentration in the substrate ranges from 0.5 to 2 g/l of the substrate.

[0009a] In an aspect, there is provided a cell culture article, comprising:

a substrate comprising a polygalacturonic acid compound selected from at least one of:

pectic acid or salts thereof, and

partially esterified pectic acid having a degree of esterification from 1 to 40 mol% or salts thereof,

wherein the polygalacturonic acid compound is crosslinked with a divalent cation and the divalent cation concentration ranges from 0.5 to 2 g/l of the substrate.

[0010] A method of making a cell culture article comprises dispensing (i.e., dropwise) a hydrocolloid solution into a gelation bath. The hydrocolloid solution comprises a polygalacturonic acid (PGA) compound selected from at least one of pectic acid or salts thereof, and partially esterified pectic acid having a degree of esterification from 1 to 40 mol% or salts thereof. The gelation bath comprises a divalent metal salt.

[0010a] In another aspect, there is provided a method of making a cell culture article, comprising:

dispensing a hydrocolloid solution into a gelation bath,

wherein the hydrocolloid solution comprises a polygalacturonic acid compound selected from at least one of:

pectic acid or salts thereof, and

partially esterified pectic acid having a degree of esterification from 1 to 40 mol% or salts thereof, and

wherein the gelation bath comprises a divalent metal salt.

[0011] A method for culturing cells comprises contacting cells with a cell culture medium having a cell culture article as described above and culturing the cells in the medium. A method for harvesting cultured cells comprises culturing cells on the surface of the cell culture described above and contacting the cultured cells with a mixture of pectinase and a chelator to separate the cells from the article.

[0011a] In another aspect, there is provided a method for harvesting cultured cells, the method comprising:

culturing cells on the surface of the cell culture article as defined above; and

contacting the cultured cells with a mixture of pectinase and a chelator to separate the cells from the cell culture article.

[0012] In embodiments, the microcarriers are transparent, enabling cell observation, and are suitable for large-scale cell propagation in chemically-defined medium or serum-supplemented medium.

[0013] Preparation of the PGA substrates is compatible with existing high throughput manufacturing processes enabling the preparation of microcarriers having a uniform size distribution. The uniform size distribution eliminates the need for an extra sieving step, which is labor intensive, time consuming, and requires additional equipment and large volumes of water and organic solvent. The presently-disclosed synthesis is not based on an emulsion process and therefore does not require the use of a surface-active agent or a high volume of organic solvents as a dispersion medium. Further, the method uses water soluble forms of calcium and therefore enables the preparation of homogeneous and transparent PGA substrates having a smooth surface that allows easy cell observation. The method is environmentally friendly and more economical than approaches based on emulsification or internal gelation.

[0014] Digestible cell culture articles are disclosed in commonly-assigned International Publication Number WO2014/209865, the contents of which are incorporated herein by reference in their entirety.

[0015] 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