

[54] **PREPARATION OF SUBSTANCES WITH ENCAPSULATED CELLS**

[75] Inventor: Franklin Lim, Richmond, Va.

[73] Assignee: Damon Corporation, Needham Heights, Mass.

[\*] Notice: The portion of the term of this patent subsequent to Oct. 5, 1999 has been disclaimed.

[21] Appl. No.: 372,835

[22] Filed: Apr. 28, 1982

**Related U.S. Application Data**

[63] Continuation-in-part of Ser. No. 243,583, Mar. 13, 1981, abandoned, which is a continuation-in-part of Ser. No. 24,600, Mar. 28, 1979, Pat. No. 4,352,883, which is a continuation-in-part of Ser. No. 953,413, Oct. 23, 1978, abandoned.

[51] Int. Cl.<sup>3</sup> ..... C12N 11/10; C12N 11/04; C12N 5/00; C12N 5/02

[52] U.S. Cl. .... 435/178; 435/182; 435/240; 435/241; 424/93; 424/DIG. 7

[58] Field of Search ..... 435/174, 177, 178, 180, 435/182, 240, 241; 424/DIG. 7, 93

**References Cited**

**U.S. PATENT DOCUMENTS**

3,522,346	7/1970	Chang	.....	435/188 X
3,725,113	4/1973	Chang	.....	424/101 X
3,730,841	5/1973	Salvatore et al.	.....	435/182
3,733,205	5/1973	Shovers et al.	.....	435/262 X
3,827,565	8/1974	Matsumura	.....	435/182 X
3,860,490	1/1975	Guttag	.....	435/182
4,138,292	2/1979	Chibata et al.	.....	435/178
4,251,387	2/1981	Cim et al.	.....	424/DIG. 7

**FOREIGN PATENT DOCUMENTS**

2835875	4/1980	Fed. Rep. of Germany	.
1600988	9/1970	France	.
1422854	1/1976	United Kingdom	.

1506112	4/1978	United Kingdom	.
1520217	8/1978	United Kingdom	.
1525665	9/1978	United Kingdom	.
1545545	5/1979	United Kingdom	.
1553190	9/1979	United Kingdom	.
1556584	11/1979	United Kingdom	.
2046271	11/1980	United Kingdom	.

**OTHER PUBLICATIONS**

Kierstan et al., The Immobilization of Microbial Cells, Subcellular Organelles and Enzymes in Calcium Alginate Gels, Biotech. and Bioeng., vol. XIX, 1977, (pp. 387-397).

Tze et al., Implantable Artificial Endocrine Pancreas Unit Used to Restore Normoglycemia in Diabetic Rat, Nature, vol. 264, 1976, (pp. 466-467).

Chang, T. M. S., Biomedical Applications of Immobilized Enzymes and Proteins, vol. I, Plenum Press, N.Y., 1977, pp. 69-90 and 147-153.

Primary Examiner—David M. Naff

Attorney, Agent, or Firm—Lahive & Cockfield

[57] **ABSTRACT**

Disclosed is a system and process for producing substances produced in cells such as antibodies and biological response modifiers. Cells which produce the substance of interest are encapsulated within semipermeable membranes having an upper limit of permeability sufficient to allow traverse of ions, amino acids and other cell nutrients and then suspended in a culture medium. Serum components or other high molecular weight materials needed for ongoing viability and normal in vitro metabolism of certain types of cells may be included within the intracapsular volume and may be excluded from the extracapsular medium by limiting the permeability of the membranes. The substance of interest collects either in the intracapsular volume or the extracapsular medium, depending on the degree of permeability of the membranes and on the molecular weight of the substance.

**25 Claims, 2 Drawing Figures**