



[54] METHODS OF INHIBITING UNDESIRABLE CELL GROWTH USING A COMBINATION OF A CYCLOCREATINE COMPOUND AND A HYPERPLASTIC INHIBITORY AGENT

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Related U.S. Application Data

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[58] Field of Search 424/649; 514/392, 514/398, 428, 210, 90, 274, 456, 460, 563, 565

[56] References Cited

U.S. PATENT DOCUMENTS

4,766,149	8/1988	Osswald et al.	514/553
5,321,030	6/1994	Kaddurah-Daouk et al.	514/275
5,324,731	6/1994	Kaddurah-Daouk et al.	514/275

FOREIGN PATENT DOCUMENTS

0 007 597	2/1980	European Pat. Off. .
WO 9208456	5/1992	WIPO .
WO 9416687	8/1994	WIPO .
WO 9416712	8/1995	WIPO .

OTHER PUBLICATIONS

Bergmann et al. . "Synthese des Kreatines aus Sarkosin und Arginin—Neue Synthese des Methylguanidins", *Z. Physiol. Chem.* 173, 80-83 (1928).

Rowley et al. "On the Specificity of Creatine Kinase, New Glycocyamines and Glycocyamine Analogs Related to Creatine", *J. Am. Chem.*, 247:5542-5551 (Oct. 1971).

McLaughlin et al., "Specificity of Creatine Kinase for Guanidino Substrates", *J. Biol. Chem.*, 247:4382-4388 (Jul. 1972).

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[57] ABSTRACT

The present invention provides for the use of creatine compounds and hyperplastic inhibitory agents for prophylactic and/or therapeutic treatments of undesirable cell growth, e.g. tumors. The present invention provides methods of using creatine compounds, in combination with a hyperplastic inhibitory agent, to inhibit the growth of undesirable cells in a subject. The present invention is based, at least in part, on the discovery that creatine compounds and hyperplastic inhibitory agents, such as inhibitory agents, additively and synergistically combine to inhibit cell growth. The present invention further pertains to compositions for inhibiting undesirable cell growth in a subject. The compositions of the present invention include an effective amount of the creatine compound and a hyperplastic inhibitory agent in a pharmaceutically acceptable carrier. Other aspects of the invention include packaged creatine compounds and inhibitory agents. The packaged compounds and agents also include instructions for using the creatine compound/inhibitory agent combination for inhibiting undesirable cell growth in a patient or instructions for using the compounds and agents, in selected quantities, in a pharmaceutically acceptable carrier.

65 Claims, 4 Drawing Sheets

