Summary of Invention

[0008a] In one aspect, there is provided the use of a non-polymeric, highly purified and heat stable oxygen carrier containing composition in the manufacture of a medicament for reducing cancerous tumor recurrence and/or minimizing tumor cell metastasis in a mammal, wherein said composition comprising a cross-linked tetrameric hemoglobin with an undetectable dimer concentration.

[0008b] In another aspect, there is provided the use of a non-polymeric, highly purified and heat stable oxygen carrier containing composition in the manufacture of a medicament for treating cancerous tissues, wherein said composition comprising a cross-linked tetrameric hemoglobin with an undetectable dimer concentration.

[0008c] In another aspect, there is provided the use of a non-polymeric, highly purified and heat stable oxygen carrier containing composition in the manufacture of a medicament for increasing oxygenation of cancerous tissues, wherein said composition comprising a cross-linked tetrameric hemoglobin with an undetectable dimer concentration.

[0008d] In another aspect, there is provided the use of a non-polymeric, highly purified and heat stable oxygen carrier containing composition in the manufacture of a medicament for reducing size of a tumor, wherein said composition comprising a cross-linked tetrameric hemoglobin with an undetectable dimer concentration.

[0008e] In another aspect, there is provided a non-polymeric, highly purified and heat stable oxygen carrier containing composition for reducing cancerous tumor recurrence and/or minimizing tumor cell metastasis in a mammal, wherein said composition comprising a cross-linked tetrameric hemoglobin with an undetectable dimer concentration.

[0009] The present invention provides a method for processing a nonpolymeric, heat stable purified cross-linked tetrameric hemoglobin suitable for use in mammals without causing severe renal injury, vascular detrimental effects and severe adverse events including death. The present invention removes the dimeric form of hemoglobin, uncross-linked tetrameric hemoglobin, phospholipids and protein impurities. Additionally, the present invention uses (1) an instant cytolysis apparatus for precise and controlled hypotonic lysis, (2) a flowthrough column chromatography, (3) a high temperature short time (HTST) apparatus for heat processing the hemoglobin solution in the purification process to remove the undesirable non-stabilized dimers of hemoglobin and to remove the protein impurities, for example immunoglobin-G, so that renal injury, vascular detrimental effects and other toxicity reactions can be avoided, and (4) an air-tight infusion bag packaging to avoid oxygen intrusion into the product.

[0010] The method includes a starting material of mammalian whole blood including at least red blood cells and plasma. Red blood cells are separated from the plasma in the mammalian whole blood followed by filtering to obtain a filtered red blood cell fraction. The filtered red blood cell fraction is washed to remove plasma protein impurities. The washed red blood cells are disrupted by a controlled hypotonic lysis for a time sufficient to lyse red blood cells without lysing white blood cells in an instant cytolysis apparatus at a flow rate of 50-1000 liters/hr. Filtration is performed to remove at least a portion of the waste retentate from the lysate. A first hemoglobin solution is extracted from the lysate.

[0011] A first ultrafiltration process is performed using an ultrafiltration filter configured to remove impurities having a higher molecular weight than tetrameric hemoglobin and to further remove any viruses and residual waste retentate from the first hemoglobin solution to obtain a second hemoglobin solution. Flowthrough column chromatography is performed on the second