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(54) Title: METHOD FOR THE PREPARATION OF A HEAT STABLE OXYGEN CARRIER-CONTAINING COMPOSITION FACILATING BETA-BETA CROSS-LINKING

(57) Abstract: Methods for preparation of a heat stable hemoglobin based oxygen-carrier-containing pharmaceutical composition such that beta-beta cross-linking is favored are provided. Using the methods of the present invention, the oxygen affinity of the resultant molecule can be controlled so that hemoglobin based oxygen carriers tailored for specific applications can be produced. Lower oxygen affinity crosslinked hemoglobin is useful for applications requiring rapid tissue oxygenation (e.g. hemorrhagic shock) while higher oxygen affinity cross-linked hemoglobin is useful for applications requiring a slower rate of oxygenation (e.g. cancer adjunct therapy). A highly purified and heat stable crosslinked non-polymeric tetrameric hemoglobin having beta- beta cross-linking of greater than 40-60% and suitable for use in mammals without causing renal injury and vasoconstriction is produced. A high temperature and short time (HTST) heat processing step is performed to effectively remove any undesired dimeric hemoglobin, non- cross-linked tetrameric hemoglobin, and plasma protein impurities.