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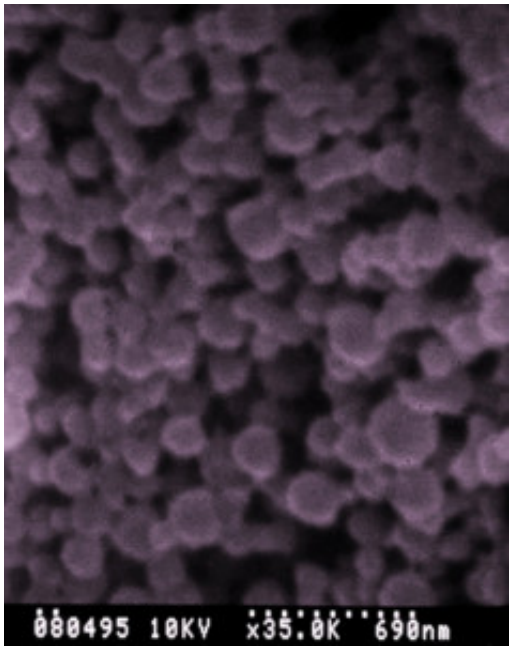
The development of a new blood substitute

The first transfusion ever performed is generally attributed to James Blundell in the beginning of the eighteenth century. Since Blundell's experiments until the beginning of the twentieth century, transfusion was considered an extremely risked procedure with general poor outcomes. However, with the advance of the knowledge about the circulatory system, especially due to Karl Landsteiner's research that lead to the discovered the ABO and Rh systems, blood transfusion became a safe procedure even though still associated with many complications. Those complications are not only related to the transfusion procedure itself but also with economic, logistic and social issues. Many complications derive from blood intrinsic characteristics such as the ability to act as an immune system suppressant after transfusion and the structural and chemical changes that blood undergo during storage. Economically, blood collecting, testing, storing and transporting is very expensive and require careful management. Beside those facts, many countries struggle with the lack of donations making blood availability difficult to manage in order to comply with the demand of the population.



Microparticles of polyhemoglobin encapsulated in gelatin. Images obtained by Scanning Electron Microscopy. Magnification of 35,000x. Resolution of 690 nm.

The development of a clinically viable blood substitute, therefore, would greatly benefit medicine and save many lives. To this purpose, one of the most successful and promising approaches to date is the use of hemoglobin based systems. Hemoglobin is a protein present in the red blood cell that is responsible for the transport of oxygen, carbon dioxide and other gases throughout the body. Once removed from the red blood cell, hemoglobin is still able to transport gases and could be used in the development of an efficient oxygen carrier system. However, hemoglobin can also provoke many deleterious effects, such as hypertension and renal failure, and therefore can not be safely injected directly into the blood. The deleterious effects of hemoglobin are mainly due to the natural ability of hemoglobin to divide itself into two dimers and the ability of hemoglobin to traverse the blood vessels wall reaching the vessels musculature and other organs. To overcome the deleterious effects of hemoglobin many approaches have been proposed. The initial proposition was to modify hemoglobin's structure by chemical means to prevent the protein to undergo division. This approach was successful in preventing renal damage but still allowed hemoglobin to traverse the vessels wall and to cause deleterious effects. Consequently a new approach was proposed, to further modify hemoglobin's structure in order to enhance the protein's dimension and, therefore, keep hemoglobin inside the vessels. This second approach evinced promising results but after several trials, it was demonstrated that the final product was still not safe enough to be introduced in medical practice and could not acquire approval from the regulatory agencies, such as the FDA. To date, innovative approaches such as the production of micro or nanoparticles are under development.

In this scope, our current research aims the development and study of a chemically modified hemoglobin encapsulated by gelatin microparticles. The proposed innovative chemical modification of hemoglobin aims to stabilize hemoglobin as a copolymer providing more spacing between the protein molecules and enhancing the overall size of the final particle while the entrapment provided by gelatin aims not only to adjust the final particle's size but also to provide structural stability and to increase hemoglobin's functional circulation time. Gelatin may also contribute to reduce the uptake of the particles by the immune system. To date, the desired chemical modifications of hemoglobin have been achieved, the encapsulation protocol developed and the initial characterization of the particle was performed. The produced particles have evinced homogeneity, stability and promising characteristics for their application in clinical practices.

Publication

Preparation and characterization of a microencapsulated polyethylene glycol cross-linked polyhemoglobin.
Knirsch MC, Dell'Anno F, Chicoma D, Stephano M, Bou-Chacra N, Palombo D, Converti A, Polakiewicz B
Bioprocess Biosyst Eng. 2015 Nov

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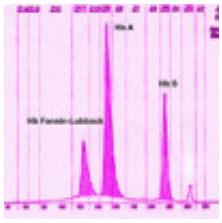

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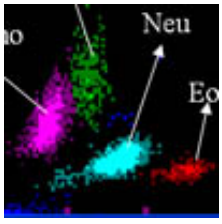

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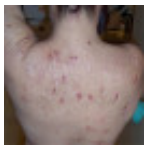

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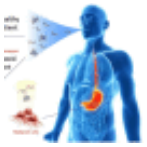

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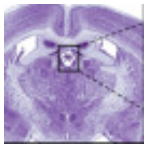

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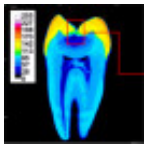

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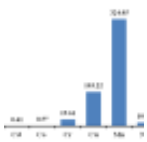

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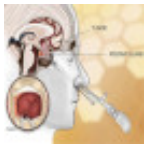

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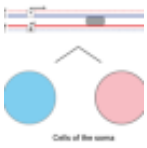

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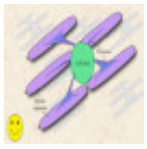

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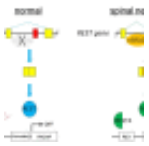

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