Sustained release of bioactive protein/drugs using amyloid hydrogel for the treatment of diabetes, arthritis, cancer and other diseases

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Specific problem being addressed: Diabetes, arthritis and cancer are some of the diseases affecting a large percentage of the Indian population. The small molecular drugs and drugs of peptide/protein origin used in their treatment require delivery by infusion, frequent injections, or subcutaneous administrations, which makes the life of the patient (especially the elderly population) miserable and non-compliant to treatment. This demands the development of a solution which is robust, tunable, scalable, and biocompatible. Continuous effort is required to improve the treatment and patient experience. In this regard, we propose a technology using amyloid delivery depot, that we have developed to provide precise delivery with minimal invasiveness, minimal immune response and long-term controlled and sustained release of the payload for the treatment of various diseases.

Project Summary: Amyloid hydrogels are hydrogels that are formed by the 3D network of protein fibrils. They have a multitude of applications in various biomedical and bio-nanotechnological fields including insulin release for the treatment of diabetes. What most of the studies failed to achieve is a long-term controlled insulin release, due to immune-response, sophisticated methods for preparation, preservation and storage. We have developed an amyloid-based hydrogel that can be used as a depot for releasing unstable proteins/drugs and also as a local delivery vehicle for small molecules in the treatment of cancer and arthritis. This system can protect the biological, physical, and chemical integrity of the drug molecule in the stable cross-β-sheet (3D network) structure without any chemical cross-linking during processing, storage, and delivery. These formulations can be easily administered subcutaneously at the desired target location. Our studies have already proven that the designed amyloid hydrogels can release insulin in a controlled and sustained manner in vitro. We have also confirmed that the insulin released from the hydrogels was biologically active and can reduce the blood glucose level upon administration.
Now we aim to evaluate the insulin release efficacy of designed functional amyloid hydrogels in vivo (diabetic animal model), modulating the mechanical and physio-chemical properties of the selected hydrogel by incorporating bio-adhesives, co-encapsulating insulin with amylin analog & animal study on the long-term toxicology effect of the developed formulation. Also, we would assess the potential of amyloid hydrogels as a local delivery system for arthritis and cancer. We have filed an Indian and US patent for the same. The future goal, however, is to perform extensive animal studies and initiate a clinical trial.

Impact of this innovation: The most important consequence of our technology is that *in case of diabetic patients, the frequency of insulin injections can be significantly reduced, thereby improving patient experience.* Secondly our technology can be reproducibly manufactured in bulk amounts at *low-cost and can therefore be afforded by low and middle income families*. The amyloid-hydrogel technology is very versatile because it can act as a drug delivery vehicle for different classes of small molecule drugs. The stable core of the hydrogel enables slow, sustained and controlled release of the encapsulated drug over a period of time. This study also led to the development of hydrogels, that could be used as an *implantable drug delivery system* in various tissues. Further, the thixotropic nature of the hydrogel serves as a perfect candidate for a long-acting storage depot without any complicated manufacturing procedure for drug loading.


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