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The effect of polysulfide-conjugation on the stability and activity of lysozyme

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Some of the most expensive medicines used today are those of enzyme replacement therapies (ERTs) for lysosomal storage diseases (LSDs) such as Gaucher's (GD) or Fabry's disease (FD). It has been found that oxidation can be a significant factor in reducing the activity of beta-glucosidase in those with GD. Moreover, in FD it has been found that anti-body formation to the exogenous enzyme can play a significant role in reducing the available enzyme as well as causing significant immunogenic side-effects. Efforts to improve the stability of the enzyme may therefore result in considerably benefits both clinically for the patients and financially for the insurance companies/care providers. In the mind-set of improving the lifespan of these enzymes, we have developed an enzyme-polymer conjugate, specifically lysozyme (a model enzyme) and an anti-oxidant polysulfide. The polymer was synthesized via anionic ring opening polymerization, and the conjugation was performed via the NHS-ester reaction to free amines (lysine) on the surface of lysozyme. The cytotoxicity of the synthesized polymer was compared to that of poly (ethylene glycol) (PEG) via MTS assay. The activities of the conjugates were performed on the lysozyme conjugates measured the lytic activity toward fluorescein-labelled Micrococcus lysodeikticus. SDS-PAGE gel electrophoresis together with MALDI-TOF mass spectrometry analysis revealed formation of conjugates of 1–3 polysulfide chains per lysozyme with only a slightly reduction in lysozyme activity. The synthesized polymer showed a toxicity profile virtually identical to PEG. Unlike the native lysozyme, the lysozyme-polysulfide conjugate was found to be resistant to oxidative denaturation and proteolysis.

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