



Novel Method of Releasing Liposomal Drugs by a Cancer-Associated Enzyme

Technology Case: RFT-0151

Invention Summary

Scientists at NDSU have recently invented a method to release drugs and other molecules from liposomes triggered by an enzyme which is responsible for cancer cell invasion and metastasis.

The uniquely-designed liposomes release the encapsulated contents in the presence of the enzyme matrix metalloproteinase-9 (MMP-9) within an hour. Other MMPs and proteolytic enzymes do not release the contents from the liposomes. The rate and the extent of contents release are easily controlled by the amount of the active enzyme and the lipid formulations of the liposomes.

In addition, inhibitors of MMP-9 can be delivered from the liposomes with a built-in "feedback" regulation.

Properties

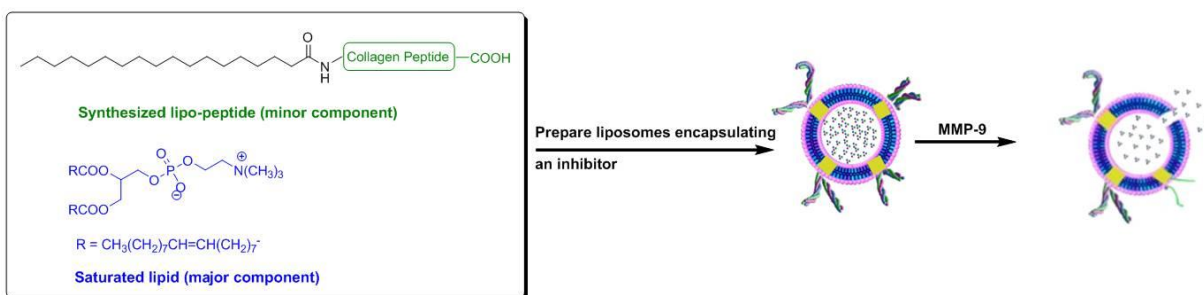
The unique design of a lipid-peptide conjugate makes the liposomes susceptible to releasing the encapsulated contents rapidly only in the presence of the cancer associated enzyme MMP-9. The designed lipid-peptide conjugate is not hydrolyzed by the general proteolytic enzymes found in human plasma.

Achieved R&D Parameters

- Fluorescence spectroscopic studies show that the liposomal contents are released within 40 minutes in the presence of cancer-associated levels of MMP-9.
- The liposome contents take 5-6 hours to release in the presence of normal levels of this enzyme in healthy persons.
- The rate and the extent of the contents release are modulated by the choice of the major phospholipid component in the liposomal formulations.
- When an inhibitor for MMP-9 is encapsulated in the liposomes, the triggered release of the contents inhibits the triggering enzyme and allows the system to operate in a self-adjusting manner.

Invention Premise

The passive release of drugs and other molecules from liposomes is a slow process. The uniquely-formulated liposomes circumvent this problem by presenting on the surface triple-helical substrate peptides for MMP-9. In the presence of elevated levels of this enzyme (as found for cancer and arthritis patients), the peptides are cleaved rapidly, leading to the liposome destabilization and release of the encapsulated contents. The liposomal formulations are non-toxic to a variety of human cell lines.



Patents

This technology is patent pending with fully preserved US patent rights available for licensing opportunities

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