Crosslinking of Water-Soluble Cyclodextrin with Hyaluronic Acid for Targeted Drug Delivery

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ABSTRACT

Introduction: Most of the cytotoxic anticancer drugs belong to substances with both low solubility in aqueous fluids and poor cellular uptake, which lead to lack of specific therapy with apparent side effects. Therefore, there is a need to develop a novel drug delivery that can remotely and selectively release their payload. Curcumin(CUR) is an antibiotic, also a powerful inhibitor of the proliferation of several tumor cells.

Aims: The aim of the present work is to highlight and discussed hyaluronic acid (HA) to be grafted with Mono-6-deoxyl-6-ethylenediamino-γ-cyclodextrin (ɣ-CD-EDA) to shape a hydrogel that ought to structure inclusion complexes with curcumin, bettering its water-solubility and serving as a model drug delivery system

Methods: Distinct copolymers had been organized HA grafted with ɣ-cyclodextrin (ɣ-CD-EDA) to form a hydrogel with various HA: ɣ-CD-EDA ratios and characterized,

by means of ^{1}H-NMR spectroscopy, zeta potential, Thermogravimetry analysis (TGA) Differential scanning calorimetry (DSC), and transmission electron microscopy (TEM). Furthermore, drug loading Encapsulation efficiency (EE%), and release kinetics, and stability. Also, cytotoxicity and uptake were assessed by flow cytometry, MTT assay and confocal laser microscopy. Wound healing activity was once improved using three cell MDA-MB-231, MCF-7, and fibroblast. Measuring the effect of HA-γ-CD-EDA1-CUR, γ-CD-EDA1-CUR, and CUR free on the Production and Secretion of inflammatory cytokines

Result: CUR loading potential used to be at once correlated with extended HA-ɣ-CD-EDA composition and morphological adjustments have been discovered upon CUR binding. The host substances and their CUR inclusion complexes are no longer cytotoxic, and consequently beneficial for CUR and drug delivery**.** Moreover, HA-γ-CD-EDA1-CUR, γ-CD-EDA1-CUR, and CUR wound healing activity was once improved, and human promonocytic THP-1 cells produce inflammatory mediators such as IL-1β, IL10,IL8, TNF-α,IRAKI and IL6 results showed that the combination HA-γ-CD-EDA$_1$-CUR could be suitable to reduce inflammation and the complex promoted the anti-inflammatory effect by the inhibition of inflammatory mediators.

Conclusion: HA grafted with ɣ-cyclodextrin (ɣ-CD-EDA) to form a hydrogel was designed, formulated, and full characterized. Nanoparticles were stable at physiological pH and have released payload. Encapsulation of CUR into polymer increased its selectivity, distribution, and accumulation into the cancer cells. HA-CD-EDA$_1$conjugated curcumin if incorporated in suitable matrix has a potential utility for treatment of wound, and down regulation in THP-1 cells.

Keywords: Cancer, Targeted Therapy, Hydrogel, Inflammation, Wound healing, Cyclodextrin, Hyaluronic.

