

Hyaluronic Acid-Amphotericin B Nanocomplexes

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Description

Natural polymer nanocomplexes systems provide pharmacotechnical benefits such as increased water solubility and reduced drug toxicity. Amphotericin B (AmB) is an anti-leishmanial and anti-fungal medication with limited water solubility and significant toxicity, which limits its therapeutic use. With this in mind, the current research intended to create nanocomplexes made of alginate (Alg), a natural polymer, with AmB covered by bacterial cellulose nanocrystals (CNC). As a result, sodium alginate and amphotericin B in a borate buffer were used to make the nanocomplexes (pH 11.0). The CNC was made by hydrolyzing bacterial cellulose with enzymes. 1 ml of nanocomplexes were added to 1 ml of 0.01 percent CNC solution to CNC cover the nanocomplexes [1].

In both formulations, the AmB complex is amorously incorporated into the polysaccharide chain network. AmB in the nanocomplexes was super-aggregated and showed good biocompatibility, being considerably less cytotoxic and hemolytic *in vitro* than the free-drug. The Alg-AmB nanocomplexes can be considered a non-toxic option to improve the AmB therapeutic impact, according to the *in vitro* toxicity studies. The entire process of obtaining nanocomplexes and coating them was carried out without the use of organic solvents, making it a green method that resulted in water soluble particles. Furthermore, CNC covering the nanocomplexes provided extra protection to the system, which could contribute to pharmaceutical innovation [2].

Amphotericin B (AmB) is a polyene antibiotic that is used to treat fungal infections as a gold standard therapy because it does not cause microbial resistance. AmB is also used to treat visceral leishmaniasis as a second-line treatment. Despite being a commonly used medicine for over half a century, AmB has significant drawbacks, including limited water solubility and permeability, as well as severe toxicity, particularly nephrotoxicity.

To overcome AmB's limitations and improve its therapeutic efficacy, drug delivery techniques are now being used. As a result, different formulations incorporating AmB, such as AMBISOME and Abelcet®, have been launched. These formulations are pricey since they are based on lipids. As a result, encapsulating AmB in a nanocomplex system consisting of a natural polymer has been discovered as a solution to the product's problem [3].

Nanocomplexes are self-organizing structures made up of a polymer (often natural polysaccharides) and a medication. This system offers several advantages, including nanoscale, high stability, superior water dispersion, low toxicity, outstanding cost-benefit, and the absence of solvents. Several studies have been published that use different types of polymers, such as dextran, gum arabic, albumin, and alginate. Alginate (Alg) is a natural polymer that is frequently employed in the pharmaceutical industry and tissue engineering. Immune system activation, nontoxicity, biocompatibility, and biodegradability

are just a few of the benefits of this substance. Bacterial cellulose nanocrystals (CNC) were used in our study to strengthen and cover the Alg-AmB system [4].

The creation of an effective amphotericin B (AmB) formulation to replace existing leishmaniasis treatments, which have major limitations, is a difficult task. We present the production of hyaluronic acid-amphotericin B self-assembled nanocomplexes (HA-AmB) utilising a simple technique that favours non-covalent drug-polysaccharide interaction in an amorphous form. *In vitro*, these water-soluble formulations with a nanometric size (300–600 nm), strong colloidal stability (zeta potential approximately 39 mV), and an AmB loading (15–18 percent) in aggregated and super aggregated forms showed less cytotoxic and hemolytic effects than the free-drug formulations. The number of intramacrophagic *L. infantum* amastigotes decreased significantly after treatment (IC₅₀ of 0.026 and 0.030 M for HA-AmB FD and HA-AmB SD, respectively), and the HA-AmB SD nanocomplex had the best selectivity index (SI) (SI of 651). Intravenous injection of the HA-AmB SD nanocomplex for three days on and three days off resulted in a significant reduction of parasites in the spleen and liver of C57BL/6 mice without the toxicity seen with free-AmB treatment. The parasite reduction found for the nanocomplex was of a comparable order of magnitude to that seen with AmBisome® in the liver. The HA-AmB SD nanocomplex's efficacy, stability, safety, and low cost point to its potential as a leishmaniasis treatment alternative [4, 5].

CNC can be utilised as a reinforcing material for drug delivery systems, protecting them and allowing for several routes of administration. CNC are made when cellulase comes into touch with bacterial cellulose. This material is renewable and sustainable, with a favourable cost-benefit ratio, biocompatibility, and biodegradability, as well as strong mechanical resistance, a wide surface area, and low toxicity. In this study, the novelties were created by coating AmB nanocomplexes with Alg and using CNC to do so. These CNC were made from bacterial cellulose that had been enzymatically degraded. As a result, we investigated the role of alginate in the creation of nanocomplexes and the CNC coat. Because there are no delivery mechanisms for Alg-AmB and CNC, the physical-chemical characteristics and *in vitro* toxicity were assessed.

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None

Conflict of Interest

The author shows no conflict of interest towards this manuscript.

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