Research Open

Nanotechnology and Advanced Material Science

Volume 2 Issue 3

Short Commentary

Nanoparticles could be a promising candidate for asthma therapy

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Received: August 22, 2019; **Accepted:** September 01, 2019; **Published:** October 06, 2019

Nanomedicine and asthma

Nanotechnology has been fundamental for respiratory medicine for various reasons; like exhibiting novel approaches in treating respiratory diseases and its applications in cosmetics, consumer products and medications which are continuously rising as well as therapeutic vaccinations. Additionally, it is being developed commercially to bring the new approach to patients [1]. Over the years many efforts are done to adopt nanotechnology for the treatment of human respiratory diseases like chronic obstructive pulmonary disease (COPD) and asthma. Asthma is a widespread heterogeneous, complex disease which affects about 300 million people around the world. This chronic inflammatory disease is characterized by airway hyperreactivity, mucus hypersecretion in the airways, and recurrent obstructive respiratory events in response to asthma "triggers [2].

Initially, asthma studies were restricted to mice, but the technology is progressing to clinical experiments. A clinical trial using nanoparticles has uncovered some of the reasons of chronic lung diseases, as ways to prevent and treat these diseases.

These nanoparticles can act as carriers for different drugs because they are so tiny to reach nearly every area and part of the human organism. Drugs can also be tied to the nanoparticles by a plenty of different linkers such as molecules or by encapsulation, which leads to better control of toxicokinetics [1].

Immunotherapy in asthma

Recently, research of allergen-specific immunotherapy (AIT) with nanoparticles (NPs) provides an effective and safe way for the treatment of allergic diseases [3]. It has been proved that encapsulation of DNA vaccines or allergens into nanostructures may provide promising results for the treatment of allergic asthma compared to the conventional AIT with noncapsulated allergen extracts [3]. Moreover, the approval of cytokine-targeting therapy like anti-IgE antibody for the treatment of asthma helped to develop novel biologicals that target T-helper Th1/Th2 interleukins; (IL)-4, IL-5, IL-13, IL-17, and IL-23 and also the epithelium-derived cytokines; IL-25, IL-33, and thymic stromal lymphopoietin [2].

PEGylated and citrated gold nanoparticles (Au)

Because of their unique and physicochemical features and availability, gold nanoparticles were used in early nanotechnology applications and stayed a contemporary research theme, with both Aurimmune (Cyt-6091) and AuroShell based on gold nanoparticles [4]. Au nanoparticles have numerous features that are attractive for use in cancer therapy; they can bind many drugs and proteins and can be targeted to tumor cells. They are tiny enough to penetrate the body and accumulate in tumors to enhance permeability and retention (EPR) effect [5].

Moreover, Omlor et al. [6] reported in their ovalbumin-induced airway inflammation study that gold nanoparticles have anti-inflammatory effect. Dispersions of both polyethylene-glycol-coated (PEGylated) and citrate/tannic-acid-coated (citrated) gold nanoparticles were applied by intranasal route to asthma and control mice. Particularly citrated gold nanoparticles inhibited both airway hyperreactivity and inflammatory infiltrates. The results suggested that gold nanoparticle-based asthma drugs could have therapeutic potential [6].

A novel anti-IL4Rα nanoparticle; superparamagnetic iron oxide nanoparticles (SPION)

Among different drug nano-carriers, superparamagnetic iron oxide nanoparticles (SPIONs) have shown promising potential in the field of nanomedicine. SPIONs have the highest drug targeting efficiency among other drug carriers, since their external magnetic surface applied to the target organs promotes the accumulation of magnetic nanoscales in the drug site of action [7].

Moreover, they have been used in preclinical applications like magnetic resonance imaging (MRI), hyperthermia, immunoassays, cell tracking, and drug delivery [8]. When iron oxide nanoparticles enter the body, they have the ability to interact with biological compounds such as proteins and cells; leading to distribution of NPs into different organs and tissues [9].

Recently, many strategies aimed to block IL4Rα, the receptor for a key pro-inflammatory pathway. Halwani et al. [10] reported that PEGylated dextran SPION conjugated to anti-IL4Rα blocking antibodies (anti-IL4Rα NPs) efficiently suppressed lung inflammation

in a mice model of asthma. Interestingly, exposure to these nanoparticles deactivated CD4 and CD8 T cells and inhibited their ability to produce pro-inflammatory cytokines in murine lung tissue. Moreover, the number of immune cells; lymphocytes, neutrophils and eosinophils were also reduced [10].

These findings suggested that biological molecules targeting IL4Rα might supply a novel therapeutic modality, mostly for patients suffering from uncontrolled, severe asthma [11] [12].

Hydroxybenzyl alcohol (HBA)-incorporated polyoxalate nanoparticles (HPOX)

p-Hydroxybenzyl alcohol (HBA) was defined as one of phenolic compounds in herbal agents and has an important role in protection against oxidative damage-relative pathologies due to its anti-inflammatory properties [13]. Yoo et al. reported a category of fully biodegradable hydroxybenzyl alcohol (HBA)-incorporated polyoxalate (HPOX) as a new therapeutics of airway inflammatory diseases [14].

This anti-asthmatic effect was shown in a mouse model by decreasing the expression of pro-inflammatory mediators like iNOS and IL-4 and the recruitment of inflammatory cells. Moreover, these nanoparticles showed high potent anti-inflammatory and antioxidant influences by decreasing the generation of oxidative stress, scavenging H_2O_2 and inhibition the expression of pro inflammatory cytokines such as IL-1β, inducible nitric oxide synthase (iNOS), and cyclooxygenase-2 (COX-2) in activated macrophages [14].

Due to their superior anti-inflammatory, antioxidant, and anti-asthmatic properties, HPOX nanoparticles could have a major potential as drug transporter and therapeutics for the handling of asthma and other airway inflammatory diseases like COPD [14].

Curcumin-solid lipid nanoparticles (curcumin-SLNs)

Curcumin has unique pharmacological properties including the anti-inflammatory effect, however, its fast metabolization and low bioavailability have restricted its usage [15]. In asthma experimental rat model, curcumin-SLNs effectively suppressed inflammatory cell infiltration and airway hyperresponsiveness and also prevented the production of Th2 cytokines, including IL-4 and IL-13 [15]. These findings suggest that curcumin-SLNs can be a potential candidate for the treatment of allergic diseases like asthma [15].

Conclusion

Asthma is a widespread, chronic inflammatory, heterogeneous, and obstructive pulmonary disease. Nanoscale based drug delivery systems can offer great potential for modern therapeutics. This work summarizes some nanoparticles that are likely to show pharmacological efficacy targeting airway inflammation.

Many promising nano based drugs are currently undergoing clinical trials to be used as novel therapies against diseases such as lung cancer, COPD, and pulmonary fibrosis.

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Citation:
Shaza Abdulnasser Harfoush, Robert Bals and Quoc Thai Dinh (2019) Nanoparticles could be a promising candidate for asthma therapy. *Nanotechnol Adv Mater Sci* Volume 2(3): 1–2.