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POLYCAPROLACTONE NANOPARTICLES OF N-ACYLHYDRAZONE DERIVATIVE FOR POTENTIAL ASTHMA TREATMENT

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ABSTRACT

BACKGROUND: Asthma is a chronic inflammatory disease of the airways that affects approximately 300 million people worldwide, with a risk of severe respiratory crises and death (Backman *et al.*, 2017). Current treatment, based mainly on corticosteroids and bronchodilators, is often associated with adverse side effects, such as generalized immunosuppression, hypertension, and long-term treatment resistance. Therefore, there is an urgent need for new therapeutic strategies that effectively control inflammation, with fewer adverse effects. 2-cyano-*N*'-(3-ethoxy-4-hydroxybenzylidene)-acetohydrazide (JR12), an *N*-acylhydrazone derivative, presents anti-inflammatory activity, selectively acting on specific inflammatory mediators, such as the pro-inflammatory cytokines TNF-α and IL-1β, without broadly suppressing the immune system, as occurs with corticosteroids (Silva, 2015). In this context, JR12 has demonstrated great potential in treating inflammatory lung diseases, such as asthma, with proven anti-inflammatory and mucolytic activities (Silva, 2019). **OBJECTIVES:** In order to improve bioavailability and provide a controlled and sustained release of the active pharmaceutical ingredient (API), this work describes the development and characterization of polycaprolactone (PCL) nanoparticles containing JR12. **METHODS:** Nanocarriers containing different concentrations of JR12 (6, 12, 30, and 50mg) were prepared using the nanoprecipitation method. The parameters size, polydispersity index (PDI), and electrokinetic potential (Zeta) were determined by Dynamic Light Scattering (DLS) using a Zetasizer ultra red; Structural integrity by infrared (IR) spectroscopy and nuclear magnetic resonance (NMR); Encapsulation efficiency was determined by the ultraviolet-visible (UV-Vis) spectroscopy. **RESULTS AND DISCUSSION:** The results demonstrated stability of the nanoparticles for up to 60 days in all concentrations of the analyzed API, with an average size of 200 nm, PDI below 0.3, Zeta potential between -16 and -30 mV, without significant changes caused by the variation in the amount of JR12, and encapsulation efficiency of 98 ± 1%. The structural characterization (Iv and NMR) confirmed the integrity of the encapsulated JR12, suggesting that suggesting that PCL nanoencapsulation of JR12 is a promissing option to optimize drug release and reduce inflammation and mucus production in the airways. **CONCLUSION:** The present work demonstrated that the formulation of PCL nanoparticles containing the *N*-acylhydrazone derivative is feasible for the nanoprecipitation method. However, aiming at the treatment of inflammatory lung diseases, additional *in vitro* and *in vivo* studies are necessary to validate the clinical efficacy and safety of this delivery system.

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