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Targeted delivery of aerosolized fisetin-loaded polymeric nanoparticles: A promising inhalation therapy for asthma

Linda Jeeva Kumari
Anna University, INDIA

Statement of the Problem: Asthma is a chronic inflammatory lung disease which is characterized by airway hyperresponsiveness, airway inflammation and goblet cell hyperplasia. It affects about 339 million people globally with an estimation of an additional 100 million asthmatics by 2025. Peroxisome proliferator-activated receptor gamma (PPARγ) is a nuclear hormone receptor that acts as a therapeutic target for asthma. PPARγ agonists are shown to combat inflammatory responses in asthma pathogenesis. Synthetic PPARγ agonists like thiazolidinediones impose various adverse effects, hence we opted for a phytocompound over conventional drugs. Fisetin, a PPARγ agonist is a highly hydrophobic flavonoid present in many fruits and vegetables that possesses anti-asthmatic property. However, poor aqueous solubility limits its pharmacological activity. Nanoparticle-based drug delivery systems are developed to target alveolar macrophages associated with pulmonary inflammation. Polymeric nanoparticles are biocompatible, safe and stable with sustained release property for better therapeutic effect. Therefore, the purpose of the study is to develop fisetin-loaded polymeric nanoparticles (Fis-Nps) and explore the anti-asthmatic effect of encapsulated fisetin over free fisetin via PPARγ-dependent pathway. Methodology & Theoretical Orientation: Fis-Nps were prepared by nanoencapsulation technique. Physiochemical characterizations, *in vitro* drug release and hemocompatibility studies were performed. *In vivo* anti-asthmatic studies of aerosolized Fis-Nps in ovalbumin-induced BALB/c mice model via inhalation route of administration were performed. PPARγ-mediated anti-asthmatic action of Fis-Nps was elucidated by protein expression studies (western blot). Findings: Inhalation administration of Fis-Nps remarkably ameliorated airway hyperresponsiveness, inflammatory cells, pro-inflammatory cytokines, nitric oxide, reactive oxygen species, eosinophil peroxidases and serum IgE, thereby attenuating the disease progression in asthma via up-regulation of PPARγ. Conclusion & Significance: Nanoencapsulated Fis-Nps exhibits better anti-asthmatic activity over free fisetin wherein PPARγ plays a master regulator. Thus, the pharmacological potential of fisetin is significantly enhanced by nanoencapsulation and the targeted delivery of aerosolized nanoformulation leads to an effective asthma control strategy.

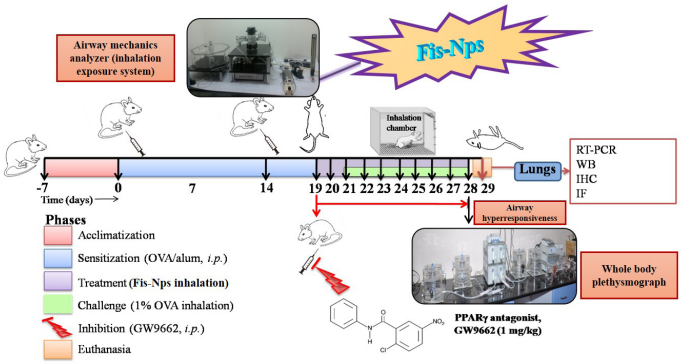

Figure 1: Schematic representation of PPARγ-dependent anti-asthmatic action of aerosolized fisetin-loaded polymeric nanoparticles (Fis-Nps) via inhalation route of administration.

Biography

Linda Jeeva Kumari Henry is a doctoral research scholar at the Department of Pharmaceutical Technology, Centre for Excellence in Nanobio Translational Research (CENTRE), University College of Engineering (UCE), Anna University, Tiruchirappalli, Tamil Nadu, India. Her specializations include pulmonary pharmacology, drug delivery, cell culture and molecular biology. She has worked as a junior research fellow in the Government of India sponsored National Facility for Drug Development, and has handled the responsibility of organizing cell culture facility, laboratory of pulmonary research. Her research focuses on developing targeted drug delivery system for the management of asthma. She has actively participated and presented papers in various national and international conferences. She has published eleven research articles in peer-reviewed journals with a cumulative impact factor of 32.459. Her passion is to explore the potentials offered by nanotechnology in the arena of translational medicine that could benefit the society, thereby improving the quality of human life.