C) Statement of research achievements, if any, on which any Fellowship has already been received by the applicant. Please also upload brief citation(s) on the research work(s) for which the applicant has already received the Fellowship(s) (not to exceed 2000 words).

The applicant has won Pharma Innova Best Research guide Award in Pharmacology Category from RV Patel, PharmaInnova Awards, Conducted by Troikaa Pharmaceuticals Limited, Ahmadabad for the year 2016. This award was given after national level competition from all the eligible M. Pharm thesis submitted byeligiblesupervisorsacross India. Our work entitled Protective effects of Nanoceria and Withaferin A in Bleomycin Induced Pulmonary Fibrosis won best M. Pharm thesis and Best M.Pharm Research guide award in Pharmacology category. The work demonstrated the potential therapeutic effects of Nanoceria (Cerium oxide nanoparticles) and Withaferin A in Bleomycin induced pulmonary fibrosis mice model. These Cerium Oxide nanoparticles were found to be highly effective in treating pulmonary oxidative stress, Inflammatory cytokines and BALF cell parameters. In addition, these nanoparticles also significantly normalized lung tissue morphology and prevented collagen accumulation in fibrotic lungs. Another promising natural product Withaferin A (WFA) also produced excellent protective effects in the Pulmonary fibrosis model.

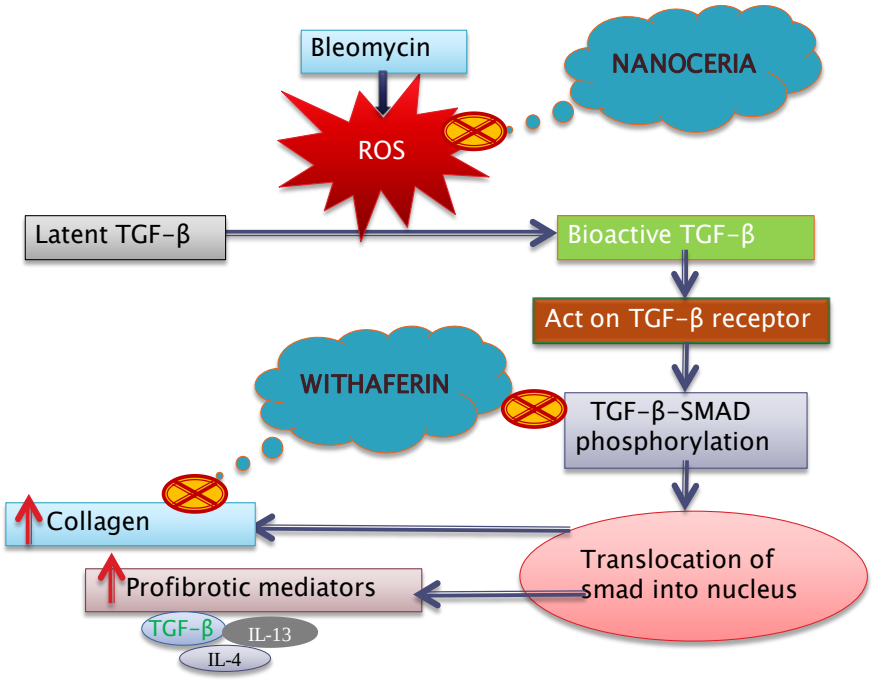

Figure 1: *Hypothesis Evaluation of Protective Effects of Nanoceria and Withaferin A (WFA) in Bleomycin induced Pulmonary fibrosis.*

Pulmonary fibrosis (PF) is a chronic slow progressive inflammatory disorder with a median survival of less than 3 years upon diagnosis. Existing treatments result in inadequate therapeutic outcome, because scarring is permanent once it has developed. Lung transplantation is so far the only treatment with proven benefit, conferring a better survival rate. Recently USFDA approved Esbriet (Perfenidone) and Ofev (Nintedanib) for the treatment of PF. However, these drugs seem to affect vital pathways. Several studies suggest that oxidative stress and inflammation plays a crucial role in inducing PF. Thus, the compounds exhibiting potent antioxidant and anti-inflammatory activity are expected to be beneficial in PF. Cerium Oxide nanoparticles (also called Nanoceria) and Withaferin A (originated from ancient Indian medicinal plant Withania Somnifera) were selected to evaluate their effect in treating PF.Due to lack effective therapeutic options, our observations indicate potential application of these highly safer trace metal based nanoceria and Natural product based Withaferin A.

The most significant outcome of this work is anti-fibrotic effects of Nanoceria and Withaferin A in lung fibrosis model. Nanoceria inhibited the expression of inflammatory cytokines and transcription factors (TGF-β) in the lung tissues. Further, it did not produce any toxic effects upon repeated Oropharyngeal administration in the lungs, which ensures the safety of this nanoparticles and Nanotoxicology concerns also not observed in nanoceria treated animals. This study also signifies the promising role of rare earth minerals in the form of nanoparticles to combat several oxidative stressinflammatory stress related conditions, which is seen not only in lung fibrosis but also seen in several disease states. Our studies also rationalizes the use of Withania somnifera extracts in several Ayurvedic products. This study also proposes that Withaferin A can be effective therapy in Pulmonary fibrosis. Moreover, Withaferin A being natural source product found to be safer in animal models.

Effect of Withaferin A on Bleomycin induced Pulmonary fibrosis: WFA treatment reduced the progression of PF by modulating the EMT related cell markers both *in vivo* and *in vitro.* WFA ameliorated the expression of inflammatory cytokines including NF-κB p65, IL-1β and TNF-α, as well as attenuated the expression of pro-fibrotic proteins including CTGF, collagen 1A2, collagen 3A1, and fibronectin. Expression of angiogenic factors like VEGF, FAK, p38 MAPK, and PLC-γ1 were also inhibited by WFA. Phosphorylation of Smad 2/3 induced by TGF-β1 and Bleomycin were significantly inhibited. WFA suppressed ECM deposition. In a nutshell, Withaferin A could probably prove as an efficient and potential therapeutic against PF.

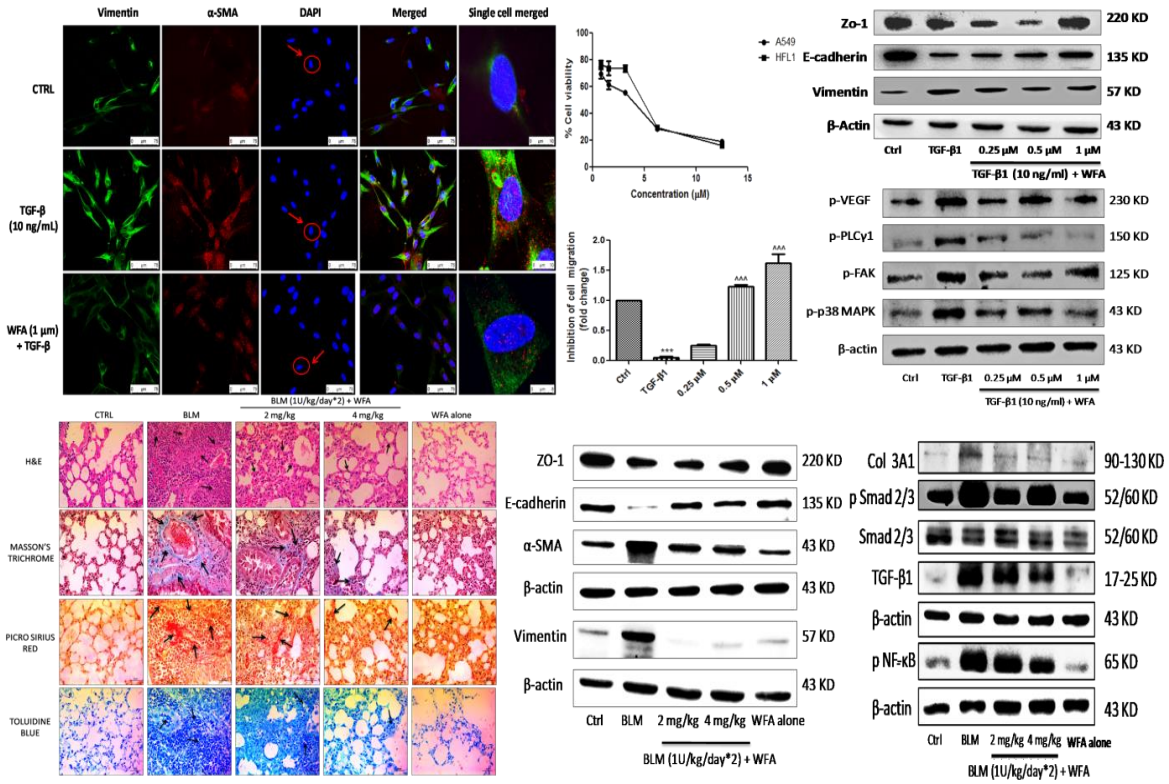

Figure 2: ***Effect of WFA in Bleomycin induced Pulmonary fibrosis.*** *(A) Effect of WFA on cell viability of A549 and HFL1 cell lines (B) Effect of WFA on cell migration on HFL1 cell lines (C) Photomicrographs exhibit staining of mice lung tissues with H&E, Masson's trichrome, PSR and toluidine blue as shown from top to bottom. Arrows indicate the extent of pathological features of respective stains (D) Immunofluoresence evidence for decreased expression of Vimentin and α-SMA proteins by WFA in lung fibroblasts (E) Effect of WFA on EMT related cell markers in vitro ZO-1, E-cadherin, Vimentin and α-SMA were studied using western blot analysis in A549 cell (F) Immunoblots of effect of WFA on angiogenic markers p-VEGF, p-FAK, p-PLCγ1, and p-38 in cell lysates of HFL1 cells (G) Effect of WFA on EMT related cell markers in vivo ZO-1, E-cadherin, Vimentin and α-SMA studied in lung tissues of all experimental groups (H) Representation of immunoblots of inflammatory and fibrotic markers pNF-κB, TGF-β1, pSmad 2/3 and COL3A1 in lung tissues of all experimental groups.*

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