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Development, optimization, evaluation of inhalable solid sedds to cure pulmonary arterial hypertension (PAH)

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Pulmonary arterial hypertension (PAH) is a rare syndrome of fatigue and dyspnoea, which is classified under Group I out of the five groups of pulmonary hypertension (PH) prescribed by WHO in which mean pulmonary arterial pressure becomes greater than 25 mm Hg at rest or 30 mm Hg during physical activity. Since the prevalence of the disease, several attempts have been made to prepare effective formulations. In order to overcome the shortcomings of the reported formulations of poor extended action, low bioavailability, reduction in systolic blood pressure, delayed onset of action and teratogenicity, the main aim of the present research work was to screen the drugs of phosphodiesterase type-5 (PDE-5) inhibitor group through computational drug development tools in order to select the best drug: tadalafil, which would increase the vasodialation of pulmonary artery thereby inhibiting vascular remodelling thus lowering the PH and subsequently pulmonary vascular resistance. In the wet lab a novel approach of inhalelable solid self emulsifying drug delivery system was selected for lung targeting. The optimized formulation was taken up for microphage uptake studies and animal studies to identify ex-vivo release and pharmacodynamics studies. The main finding of the research was that the optimized formulation showed much higher vasodialatory effect based on intratracheal catharization ranging from 240 nm to 280 nm as compared to pure drug ranging form 11 nm to 15 nm. The high macrophage intake capacity of 6% as compared to pure tadaladil 0.25% helped to increase the bioavlability of the drug.

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