Original Article

Exploring the potential of Beta- 2 Agonist, Salbutamol Against Muscle Atrophy Using Computational Approach

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DOI: 10.47750/pnr.2022.13.S05.417

Abstract

Background: Muscle atrophy affects many individuals every year, and there are only a few FDA-approved drugs to treat skeletal muscle wasting. This is caused by a combination of factors including inactivity, aging, and a wide range of diseases such as diabetes, cancer, neurodegenerative disorders, bacterial and viral infections, chronic respiratory and renal diseases, and several drug side effects.

Aim: Therefore, the present study was aimed to evaluate the anti-muscle atrophy potential of existing beta 2 agonist, salbutamol through *in silico* approach.

Methods: Solubility analysis of salbutamol was performed in different solvents *i.e.* water, ethanol, ether, HCl, and chloroform to confirm the solubility behaviour. Calibration curve of salbutamol was prepared in 0.1N HCl (276 nm) and assessed by UV spectroscopy. Fourier transform infrared spectroscopy (FTIR) analysis of salbutamol was performed to confirm the purity of salbutamol. Furthermore, molecular docking was performed using the Autodock Vina software to confirm the affinity of ligand-protein complexes (AKT1, Growth differentiation factor 8 (GDF-8), IGF-1, MuRF-1, MyoD, and TNF-α).

Results: Solubility results showed that salbutamol was sparingly soluble in water and ether, freely soluble in 0.1 N HCl solutions, and also in ethanol and chloroform which indicates the drug is highly soluble. The calibration curve uses to assess the amount of drug in plasma a different time interval. FTIR results of salbutamol showed sharp peaks at 4000-400 cm^{-1} wavelengths. The molecular docking shows the high binding energy with the target protein *viz.* AKT1, Growth differentiation factor 8 (GDF-8), IGF-1, MuRF-1, MyoD, and TNF

Conclusions: Results demonstrate that β2-adrenergic agonist salbutamol shows good binding affinity to catabolic (MuRF-1, myostatin, MyoD and TNF-α) and anabolic proteins (AKT1, IGF-1, and GDF-8) through a computational approach to predict the skeletal muscle atrophy.

Keyboards: Skeletal muscle atrophy, Beta2-agonist, molecular docking, AKT1 and MuRF-1

INTRODUCTION

Skeletal muscle atrophy is a common illness condition caused by inactivity, aging, and diseases including sepsis, diabetes, cachexia and side effects of drugs (Cohen et al., 2015). Muscle mass and function loss ultimately affects the quality of life by increasing morbidity and mortality. Exercise, acupuncture has been recognised for anti-muscle atrophy measure to treat muscle wasting. The last ten years have seen a number of studies illuminate the underlying molecular pathways, opening the door to the development of new medications for muscle atrophy (Sartori et al., 2021). According to studies, the retrieval of both agonists and beta blockers performed exceptionally well when individual docking experiments were combined with receptor ensemble docking (Costanzi & Vilar, 2012). Based on predictions of the energy of the binding protein-ligand interactions and modes of action, pharmacological agents for different diseases could be screened using molecular docking. The targeted binding site of a protein is computationally modelled for ligand binding poses, and poses are then optimised to provide structural information and activity predictions in the form of thermodynamic binding affinities. The process of "reverse docking," in which a small molecule is docked across different potential protein targets, uses docking to uncover binding partners and drug mechanisms of action. In "one target, many compounds" approaches, docking was used to enrich for potential hit substances that bind pre-specified proteins (Meng et al., 2011). Salbutamol (SLB) is a short acting of synthetic selective to β2-adrenoceptors agonist traditionally used as bronchodilator for treatment of bronchial associated with asthma and symptomatic patients with COPD. SLB is similar chemical structure with of adrenaline derived by catecholamine act as neurotransmitter (Hostrup et al., 2018). As epinephrine and β2-agonists prevent protein degradation in isolated rat muscles, and showed direct