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Recent Advances in Process Development of Antiviral Agents Targeting the Influenza Virus: Amantadine-Remantadine-Derived Pharmaceutical Agents

Pathy KS*

Department of Chemistry, IPL research center Lucknow, India

***Corresponding author:** Krishna Sarma Pathy, Department of Chemistry, IPL research center Lucknow, India, Tel: 9919188895; Email: drkrishnasarmapathy@yahoo.in

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Abstract

This short review summarizes our work on the process development for the synthesis of amontidine remantadine. The M2 proton channel of the influenza A virus is the target of the anti-influenza drugs amantadine and rimantadine. The effectiveness of these drugs has been dramatically limited by the rapid spread of drug resistant mutations, mainly at sites S31N, V27A and L26F in the pore of the channel. Despite progress in designing inhibitors of V27A and L26F M2, there are currently no drugs targeting these mutated channels in clinical trials. The article traces the evolution of various synthesis approaches and provides a comparison for overall yield efficiency. Amantadine hydrochloride is an antiviral drug used in prevention and treatment of influenza a infections. It has also been used for alleviating early symptoms of Parkinson's disease. Several methods for the preparations of Amantadine hydrochloride have been reported. Overall yields ranging from 50 to 52%. In this article, we describe procedure for the synthesis of Amantadine hydrochloride from via N-(1-adamantyl) acetamide with an improved yield of 60% the procedure was also optimized to reduce the use of toxic solvents and reagents, rendering it more environment-friendly. The procedure can be considered as suitable for large-scale production of amantadine hydrochloride.

Introduction

It is estimated that over 40 million people perished during the 1918 Spanish influenza pandemic, and nearly 35% of the global population was infected with the disease [1]. From Europe to America and even reaching as far as the wilderness of Alaska and remote Pacific islands, this virus was exceptionally widespread during a time when global travel was not very prominent. This pandemic has been regarded as one of the single most devastating infectious disease events in recorded history [1]. It is currently believed that the influenza strain responsible for the 1918 Spanish flu is genetically linked to the N1H1 influenza that emerged in 2009 and threatened another pandemic [1,2]. With the advent of modern vaccinations, the death toll from the flu virus has been substantially lowered, but there still remains the possibility for a recurrent epidemic. Should the virus mutate in such a way that a new variant circulates, there