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Strategies for ribavirin prodrugs and delivery systems for reducing the side-effect hemolysis and enhancing their therapeutic effect

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Abstract

Ribavirin is a nucleoside which is used as an antiviral agent against both RNA and DNA viruses. However, accumulation in erythrocytes causes hemolysis which limits its usefulness. To minimize ribavirin-induced hemolysis and increase its antiviral effect, considerable efforts have been made involving chemical prodrugs and various formulations. Combination with macromolecules to achieve better targeting and increased uptake is one of the most promising strategies. In addition, decreasing the association with RBCs through prodrugs and delivery systems is considered. This review summarizes prodrugs and delivery systems for ribavirin and, at the same time examines these different strategies. Moreover, a novel design of prodrug is proposed for further study.

Keyword: ribavirin; hemolysis; antiviral effect; prodrug; delivery system

1. Introduction

Ribavirin(1-b-D-ribofuranosyl-1,2,4-triazole-3-carboxamide), a synthetic nucleoside, exhibits a broad spectrum of activity against DNA and RNA viruses[1], mainly including respiratory syncytial virus[2] and lassa fever virus[3], in addition to its combination with peg-interferon , a standard therapy for chronic Hepatitis C[1, 4] in clinical situations. The FDA approved treatment for chronic hepatitis C virus (HCV) is the combination of pegylated interferon-α (IFN), ribavirin and protease inhibitors such as boceprevir and telaprevir[5]. With the advent of direct-acting antiviral (DAA)