Pharmacological Reports
2011, 63, 601–617
ISSN 1734-1140

Review

Therapeutic potential of adenosine analogues and conjugates

Monika Samsel, Krystyna Dzierzbicka

Department of Organic Chemistry, Gdansk University of Technology, G. Narutowicza 11/12, PL 80-952 Gdańsk, Poland

Correspondence: Monika Samsel, e-mail: s.monika@wp.pl

Abstract:
This review summarizes current knowledge of adenosine analogues and conjugates with promising therapeutic properties. Adenosine is a signaling molecule that triggers numerous physiological responses. It acts through the adenosine receptors (ARs), belonging to the family of G-protein-coupled receptors and widely distributed throughout the body. Moreover, adenosine is involved in key biochemical processes as a part of ATP, the universal energy currency. Thus, compounds that are analogues of adenosine and its conjugates have been extensively studied as potential therapeutics. Many inhibitors of ARs are in clinical trials as promising agents in treatment of inflammation, type 2 diabetes, arrhythmia and as vasodilators used in the myocardial perfusion imaging (MPI) stress test. Furthermore, adenosine analogues revealed high efficacy as enzyme inhibitors, tested for antitrypanosomal action and as bivalent ligands and adenosine-oligoarginine conjugates as inhibitors of protein kinases.

Key words:
adenosine, adenosine conjugates, adenosine receptors, inhibitors of protein kinases

Abbreviations: AdoMetDC – S-adenosylmethionine decarboxylase, AR – receptor for adenosine, β_2AR – β_2-adrenergic receptor, FFA – free fatty acids, GMC – glomerular mesangial cells, HAT – Human African Trypanosomiasis, IP – ischemic pre-conditioning, MPI – myocardial perfusion imaging, NEFA – nonesterified fatty acid, PK – protein kinase, T2D – type 2 diabetes, TG – triglycerides

Introduction

Adenosine (Fig. 1) is an endogenous purine nucleoside that plays an important role in the human body. It is present constitutively at a low level extracellularly (revised 1 μM), but its concentration increases under metabolic stress (e.g., hypoxia and ischemia) [56]. Adenosine acts through the adenosine receptor (AR) belonging to the family of G-protein-coupled receptors. So far, four subtypes of ARs (i.e., adenosine A_1, A_{2A}, A_{2B} and A_3 receptors) have been recognized [39]. The binding of adenosine to A_1 and A_3 receptors inhibits adenylyl cyclase activity, and binding to A_{2A} and A_{2B} subtypes causes an increase in cAMP concen-

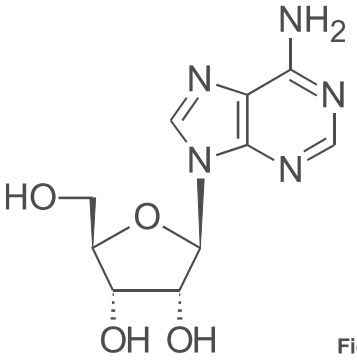

Fig. 1. Adenosine structure