

Drug evolution: p-aminobenzoic acid as a building block.

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Streszczenie

The core or the building block is an important component in drug development. In this article, we propose and review p-aminobenzoic acid (PABA) as a building block used in the design of drugs or drug candidates. PABA is frequently found as a structure moiety in drugs. For example, in a database of 12,111 commercial drugs, 1.5% (184 drugs) were found to contain the PABA moiety. These drugs have a wide range of therapeutic uses, such as: sun-screening, antibacterial, antineoplastic, local anesthetic, anticonvulsant, anti-arrhythmic, anti-emetic, gastrokinetic, antipsychotic, neuroleptic, and migraine prophylactic. This article reviews the molecular targets and the mechanisms of these activities. Drugs containing PABA also show a wide range of structural diversity. Of the 184 PABA containing drugs identified, 95 different substitutions were found at the carboxylic group and 61 were found at the amino group of the building block. Substitution on the aromatic ring was also diverse. 13, 3, and 13 different side chains were found to modify positions 2, 3 and 5 of the aromatic ring respectively. In some drugs, the amino group is further substituted to form tertiary amine (4 different side chains). Substitutions at the carboxyl and amino groups of PABA are particularly suitable for the generation of combinatorial libraries. Just by reshuffling the identified side chains of the 184 PABA containing drugs, 4.5 million compounds can be generated. Consequently, PABA fits well as a building block for a general chemical library of "drug-like" molecules with a wide range of functional and structural diversity.

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