2. Abstract

Thymidine phosphorylase (TPase), also known as gliostatin or Platelet-derived endothelial cell growth factor (PD-ECGF), is an enzyme with an important role in the nucleoside metabolism and is also involved in degradation and recycling of DNA. TPase catalyzes the reversible phosphorolysis of pyrimidine 2´-deoxynucleosides to 2-deoxy-D-ribose-1-phosphate and their respective bases, as well as the transfer of the deoxyribosyl moiety from one pyrimidine base to another.

Thymidine phosphorylase is a therapeutic target of great importance because of its participation in angiogenesis especially in solid tumors of various tissues. Therefore, TPase stimulates tumor growth and progression, as well as metastasis. In addition to this, TPase inhibits apoptosis, particularly of tumor cells and causes degradation of several antiviral and anticancer drugs. Apart from the carcinoma tissues, thymidine phosphorylase is overexpressed in various other tissues affected by disorders characterized by proliferation of blood vessels including psoriasis, rheumatoid arthritis and atherosclerosis.

Inhibiting the activity of TPase selectively in the tissues affected by the diseases listed above would be of great therapeutic significance. Therefore, many inhibitors, mainly substrate analogues, have been designed based on the knowledge of the enzyme's detailed structure. These inhibitors are listed and discussed in this thesis.