INTRODUCTION

$K^+$ channels determine the resting membrane potential and cellular excitability of most cells [1]. The opening of $K^+$ channels shifts the membrane potential towards the $K^+$ equilibrium potential which is around -90 mV. In excitable cells endowed with depolarization-activated $Ca^{2+}$ channels (voltage-gated $Ca^{2+}$ channels, VOCCs), hyperpolarization will prevent such channels from opening and block $Ca^{2+}$ entry via this pathway. In cells devoid of VOCCs or in cells where these channels are not important for $Ca^{2+}$ entry, e.g. endothelial cells, leukocytes and others, hyperpolarization will increase the driving force for $Ca^{2+}$ entry into the cell and promote $Ca^{2+}$ influx into the cell via pathways which are active at such hyperpolarized membrane potentials [2]. In this article we will shortly review the major classes of $K^+$ channels and consider their physiological role in vascular smooth muscle cells, endothelial cells and macrophages. Emphasis will be placed on vascular ATP-sensitive $K^+$ channels ($K_{ATP}$ channels) and their modulation in normal and pathological states.
MAJOR CLASSES OF K⁺ CHANNELS

Most K⁺ channels known to date show a fourfold symmetry, their pore forming (α-) subunits being assembled in form of a tetramer [1,3]; this basic unit is often complemented by additional subunits (termed β-, γ-, δ- etc subunits) which are important for modulation of channel activity. There are two different types of K⁺ channel α-subunits which are characterized by the number of α-helical segments spanning the membrane and which determine whether the channel falls into the superfamily of the voltage-gated or the inwardly rectifying K⁺ channels (K₁R) (Fig. 1).

α-subunits of K₁R channels contain two transmembrane segments (M1 and M2) which are linked by an extracellular loop (H5); this loop folds back into the membrane and contributes to the lining of the channel pore (Fig. 1). The cardiac KATP channel appears to belong to this superfamily (see below). α-subunits of voltage-gated K⁺ channels have 6 transmembrane segments designated S1 to S6 with the H5 loop connecting S5 and S6 ([1,3], Fig. 1); the S4 segment consists of four to five motifs where two hydrophobic amino acids are followed by a positively charged one generating a strong dipole moment in the membrane. Therefore, the S4 segment is supposed to constitute the voltage sensor of the channel which triggers the conformational changes leading to channel opening upon depolarization [1,3]. The S4 segment may have additional (structural) functions and, in some cases, it confers only a weak voltage dependence to the channel which is gated by other mechanisms like e.g. cyclic nucleotide binding (cyclic nucleotide-gated cation channel) [4].

Voltage-dependent K⁺ channels

Functionally, voltage-gated K⁺ channels fall into two broad categories, i.e. channels which open rapidly in response to depolarization and inactivate quite rapidly again if depolarization is sustained (A channels, Kₐ), and channels which may open more slowly and inactivate much more slowly (delayed rectifier K⁺ channels, Kᵥ); some of these Kᵥ channels do not inactivate at all over many minutes [1,3].