Large conductance calcium activated potassium channels as a drug target

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In the last ten years, Ca^{2+} activated K^+ (K_{Ca}) channels as potential targets of drug development have been continuously hot issue. Among three subtypes of K_{Ca} channels, large conductance K_{Ca} (BK) channel is genetically and also electrophysiologically resolved from other two types (small and intermediate-conductance K_{Ca} channels, SK and IK). The activation of BK channels shows voltage-dependence in addition to Ca^{2+} dependence. BK channel ß-subunit is uniformly encoded by single clone, slo, while 4 subtypes of ß subunit have been identified and found to be responsible for tissue specific differences in characteristics of BK channels. In smooth muscles, where BKß1 is predominantly expressed, opening of BK channels reduces overactivity of muscles in diseases, such as hypertention, asthma and bladder incontinent, suggesting BK channel as a potential drug target. BK channel opener may be also effective to reduce damages after ishchemia in CNS, where BKß4 is predominant. Moreover, the functional existence of BK channels with BKß1 has been revealed in cardiac mitochondria and their activation may have protective effects against ischemia similar to preconditioning. Although BKß subunits are, therefore, considered to be potential targets of drug development, BK channel openers specific to one of ß subunits have not been found. We introduce here pharmacology of some BK channel openers, including a novel ß1 specific opener.