Plantas que possuem efeito antagonista dos canais de cálcio

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Aipo – Apium graveolens


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The effect of apigenin, isolated from Apium graveolens, on the contraction of rat thoracic aorta was studied. Apigenin inhibited the contraction of aortic rings caused by cumulative concentrations of calcium (0.03-3 mM) in high potassium (60 mM) medium, with an IC50 of about 48 microM. After pretreatment it also inhibited norepinephrine (NE, 3 microM)-induced phasic and tonic contraction in a concentration (35-140 microM)-dependent manner with an IC50 of 63 microM. At the plateau of NE-induced tonic contraction, addition of apigenin caused relaxation. This relaxing effect of apigenin was not antagonized by indomethacin (20 microM) or methylene blue (50 microM), and still existed in endothelial denuded rat aorta or in the presence of nifedipine (2-100 microM). Neither cAMP nor cGMP levels were changed by apigenin. Both the formation of inositol monophosphate caused by NE and the phasic contraction induced by caffeine in the Ca(2+)-free solution were unaffected by apigenin. 45Ca2+ influx caused by either NE or K+ was inhibited by apigenin concentration-dependently. It is concluded that apigenin relaxes rat thoracic aorta mainly by suppressing the Ca2+ influx through both voltage- and receptor-operated calcium channels.

Alecrim de Jardim – Rosmarinus officinalis


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The effects of the volatile oil of Rosmarinus officinalis leaves on the tracheal smooth muscle of rabbit and guinea pig were tested in vitro using isolated tracheal strips. The volatile oil of R. officinalis leaves inhibited the contractions of rabbit tracheal smooth muscle induced by acetylcholine stimulation and the contractions of guinea pig tracheal smooth muscle induced by histamine stimulation. Also, the volatile oil inhibited the contractions of rabbit and guinea pig tracheal smooth muscle induced by high potassium (K+). This inhibition was dose-dependent and reversible. Furthermore, the volatile oil inhibited the contractions of rabbit and guinea pig tracheal smooth muscle induced by acetylcholine and histamine stimulation, respectively, in Ca(2+)-free solution. These data suggest that the volatile oil of R. officinalis leaves has a calcium antagonistic property.

Angelica – Angelica archangelica


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Twenty solvents were tested in the extraction of compounds from the roots of Angelica archangelica L. (Apiaceae), and the calcium-antagonistic activity of the extracts was investigated. Special attention was paid to the physical and chemical properties of the solvents and their extraction abilities. The calcium antagonistic effect of the extracts was investigated by measuring the inhibition of depolarization-induced Ca2+ uptake in rat pituitary GH4C1 cells. The criteria used in determining the best solvents for the extraction were the yield and the biological activity of the extract, as well as the amount of nonpolar compounds in the extract. The final criterion used in selecting the solvent was its usability with reference to boiling point, chemical interactions (e.g. methylation), etc. Chloroform was found to be the best solvent for the extraction of nonpolar, biologically active compounds from the roots of A. archangelica.

Plantas que contém ácido abscísico

Ca2+ channels at the plasma membrane of stomatal guard cells are activated by hyperpolarization and abscisic acid.

Proc Natl Acad Sci U S A;97(9):4967-72, 2000 Apr 25. Hamilton DW; Hills A; Kohler B; Blatt MR

Resumo: In stomatal guard cells of higher-plant leaves, abscisic acid (ABA) evokes increases in cytosolic free Ca(2+)-concentration ([Ca(2+)](i)) by means of Ca(2+) entry from outside and release from intracellular stores. The mechanism(s) for Ca(2+) flux across the plasma membrane is poorly understood. Because [Ca(2+)](i) increases are voltage-sensitive, we suspected a Ca(2+) channel at the guard cell plasma membrane that activates on hyperpolarization and is regulated by ABA. We recorded single-channel currents across the Vicia guard cell plasma membrane using Ba(2+) as a charge-carrying ion. Both cell-attached and excised-patch measurements uncovered single-channel events with a maximum conductance of 12.8 +/- 0.4 pS and a high selectivity for Ba(2+) over K(+) and Cl(-). Unlike other Ca(2+) channels characterized to date, these channels rectified strongly toward negative voltages with an open probability (P(o)) that increased with [Ba(2+)] outside and decreased roughly 10-fold when [Ca(2+)](i) was raised from 200 nM to 2 microM. Adding 20 microM ABA increased P(o), initially by 63- to 260-fold; in both cell-attached and excised patches, it shifted the voltage sensitivity for channel activation, and evoked damped oscillations in P(o) with periods near 50 s. A similar, but delayed response was observed in 0.1 microM ABA. These results identify a Ca(2+)-selective channel that can account for Ca(2+) influx and increases in [Ca(2+)](i) triggered by voltage and ABA, and they imply a close physical coupling at the plasma membrane between ABA perception and Ca(2+) channel control.

Capsaicina
The capsaicin receptor: a heat-activated ion channel in the pain pathway.
Nature;389(6653):816-24, 1997 Oct 23. Caterina MJ; Schumacher MA; Tominaga M; Rosen TA; Levine JD; Julius D

Resumo: Capsaicin, the main pungent ingredient in 'hot' chilli peppers, elicits a sensation of burning pain by selectively activating sensory neurons that convey information about noxious stimuli to the central nervous system. We have used an expression cloning strategy based on calcium influx to isolate a functional cDNA encoding a capsaicin receptor from sensory neurons. This receptor is a non-selective cation channel that is structurally related to members of the TRP family of ion channels. The cloned capsaicin receptor is also activated by increases in temperature in the noxious range, suggesting that it functions as a transducer of painful thermal stimuli in vivo.

Panax ginseng
Ginseng root extract inhibits calcium channels in rat sensory neurons through a similar path, but different receptor, as mu-type opioids.
J Ethnopharmacol;42(1):45-51, 1994 Mar. Nah SY; McCleskey EW

Resumo: The effect of Panax ginseng root extract on Ca2+ current of adult rat trigeminal ganglion neurons was investigated using whole-cell patch-clamp methods. The application of P. ginseng root extract (100 micrograms/ml) produced rapid, reversible reduction of the Ca2+ current by 22 +/- 4%. Treatment with pertussis toxin (250 ng/ml) for 16 h reduced the inhibition to 4 +/- 1%. The continual presence of 1 microM DAGO, a selective mu-opioid agonist that inhibits Ca2+ channels, occluded further inhibition of Ca2+ current by P. ginseng root extract. Yohimbine, phaclofen, atropine, and naloxone--antagonists of alpha 2-adrenergic, GABAB, muscarinic, and opiate receptors--did not block the inhibitory effect on Ca2+ current of P. ginseng root extract. Thus, P. ginseng root extract acts on sensory neurons through a similar pathway as mu-type opioids: both inhibit Ca2+ channels through pertussis toxin-sensitive GTP-binding proteins. However, the receptor for P. ginseng root extract is not an alpha 2-adrenergic, GABAB, muscarinic, or opioid receptor.

Effects of ginsenosides on Ca2+ channels and membrane capacitance in rat adrenal chromaffin cells.
Brain Res Bull;46(3):245-51, 1998 Jun. Kim HS; Lee JH; Goo YS; Nah SY

Resumo: We investigated the effects of ginseng total saponins (GTS) and five ginsenosides on voltage-dependent Ca2+ channels and membrane capacitance using rat adrenal chromaffin cells. In this study, cells were voltage-clamped in a whole-cell recording mode and a perforated patch-clamp technique was used. The inward Ca2+ currents (I(Ca)) was elicited by depolarization and the change in cell membrane capacitance (deltaCm) was monitored. The application of GTS (100 microg/ml) induced rapid and reversible inhibition of the Ca2+ current by 38.8 +/- 3.6% (n = 16). To identify the particular single component that seems to be responsible for Ca2+ current inhibition, the effects of five ginsenosides (ginsenoside Rb1, Rc, Re, Rf, and Rg1) on the Ca2+ current were examined. The inhibitions to the Ca2+ current by Rb1, Rc, Re, Rf, and Rg1 were 35.3 +/- 5.5% (n = 7); 41.8 +/- 7.0% (n = 8); 40.5 +/- 5.9% (n = 9); 51.2 +/- 7.6% (n = 9); and 35.9 +/- 5.1% (n = 10), respectively. The inhibitory potencies of the ginsenosides on deltaCm were Rf > Rc > Re > Rg1 > Rb1. A software based phase detector technique was used to monitor membrane capacitance change (deltaCm). The application of GTS (100 microg/ml) induced inhibitory effects on deltaCm by 60.8 +/- 9.7% (n = 10). The inhibitions of membrane capacitance by Rb1, Rc, Re, Rf, and Rg1 were 36.9 +/- 2.4% (n = 7); 36.1 +/- 1.9% (n = 12); 19.0 +/- 2.5% (n = 10); and 16.3 +/- 1.6% (n = 15), respectively. The order of inhibitory potency (100 microM) was Rc > Re > Rf > Rg1 > Rb1. Therefore, we found that GTS and ginsenosides exerted inhibitory effects on both Ca2+ currents and deltaCm in rat adrenal chromaffin cells. These results suggest that ginseng saponins regulate catecholamine secretion from adrenal chromaffin cells and this regulation could be the cellular basis of antistress effects induced by ginseng.

[Mh] Termos MeSH: Glândulas Supra-Renais/CY/ME/*PH

Ginsenoside Rf, a trace component of ginseng root, produces antinociception in mice.
Brain Res;792(2):218-28, 1998 May 11. Mogil JS; Shin YH; McCleskey EW; Kim SC; Nah SY

Resumo: Ginseng root, a traditional oriental medicine, contains more than a dozen biologically active saponins called ginsenosides, including one present in only trace amounts called ginsenoside-Rf (Rf). Previously, we showed that Rf inhibits Ca2+ channels in mammalian sensory neurons through a mechanism requiring G-proteins, whereas a variety of other ginsenosides were relatively ineffective. Since inhibition of Ca2+ channels in sensory neurons contributes to antinociception by opioids, we tested for analgesic actions of Rf. We find dose-dependent antinociception by systemic administration of Rf in mice using two separate assays of tonic pain: in the acute phase of the formalin test, and the thermal (49 degrees C) tail-flick and increasing-temperature (3 degrees C/min) hot-plate tests. The simplest explanation is that Rf inhibits tonic pain without affecting acute nociception measured in three assays of acute pain: the acute phase of the formalin test, and the thermal (49 degrees C) tail-flick and increasing-temperature (3 degrees C/min) hot-plate tests. The simplest explanation is that Rf inhibits tonic pain without affecting acute pain, but other possibilities exist. Seeking a cellular explanation for the effect, we tested whether Rf suppresses Ca2+ channels on identified nociceptors. Inhibition was seen on large, but not small, nociceptors. This is inconsistent with a selective effect on tonic pain, so it seems unlikely that Ca2+ channel inhibition on primary sensory neurons can fully explain the behavioral antinociception we have demonstrated for Rf.

Single calcium channel analysis and electron spin resonance (ESR) spectral study on the myocardial effects of ginsenoside Rb2
Zhongguo Zhong Yao Za Zhi;19(10):621-4, 640, 1994 Oct Wang XM; Qi Y; Sun CW; Zhong GG; Jiang Y; Qiu YH

Resumo: Based on the patch clamp technique, the effect of ginsenoside Rb2 on the single channel activity of Ca2+ was observed through the single ventricular myocytes of Wistar rats. Electron spin resonance was used to measure the free radical contents of the cell. It is proved that Rb2 can inhibit the activities of the single Ca2+ channel and significantly antagonize the increase of free radical contents induced by xanthine-xanthine oxidase.

Desmodium adscendens
An activator of calcium-dependent potassium channels isolated from a medicinal herb.
Biochemistry;32(24):6128-33, 1993 Jun 22. McManus OB; Harris GH; Giangiacomo KM; Feigenbaum P; Reuben JP; Addy ME; Burk DF; Kaczorowski GJ; García ML
Plantas chinesas

Plant-derived drugs acting on cellular Ca2+ mobilization in vascular smooth muscle: tetramethylpyrazine and tetrandrine.

**Effects of yixintong on regulating cellular calcium channels**

Zhongguo Zhong Yao Za Zhi;28(8):754-6, 2003 Aug. Li SC; Huang H; Zheng FM; Wen DL; Mo SW

**Nigella sativa**

Possible mechanism(s) for relaxant effect of aqueous and macerated extracts from Nigella sativa on tracheal chains of guinea pig.


**Resumo: Large-conductance calcium-dependent potassium ( maxi-K ) channels play an important role in regulating the tone of airway smooth muscle and the release of bronchoconstrictive substances from nerves in the lung. Crude extracts of Desmodium ascendens, a medicinal herb used in Ghana as a treatment for asthma, inhibit binding of monoiodotyrosine charybotoxin (125I-ChTX) to receptor sites in bovine tracheal smooth muscle membranes that have been shown to be associated with maxi-K channels. Using this assay, three active components have been purified and identified by NMR and MS. Comparison with authentic samples revealed the three active components as the known triterpenoid glycosides dehydrosoyasaponin I (DHS-I), soyasaponin I, and soyasaponin III. The most potent of these compounds, DHS-I, is a partial inhibitor of 125I-ChTX binding (Ki = 120 nM, 62% maximum inhibition). Inhibition of 125I-ChTX binding is primarily due to a decrease in the observed maximum number of binding sites, with a smaller decrease in affinity. DHS-I increases the rate of toxin dissociation from its receptor, suggesting that modulation of ChTX binding occurs through an allosteric mechanism. DHS-I reversibly increases the open probability of maxi-K channels from bovine tracheal smooth muscle incorporated into planar lipid bilayers when applied to the intracellular, but not the extracellular, side of the membrane at concentrations as low as 10 nM. In contrast, DHS-I had no effect on several other types of potassium channels or membrane transporters. This natural product is the first example of a high-affinity activator of calcium-dependent potassium channels and is the most potent known potassium channel opener.
Fissistigma glaucescens

Electrophysiological mechanisms for antiarrhythmic efficacy and positive inotropy of liriodenine, a natural aporphine alkaloid from Fissistigma glaucescens.

Br J Pharmacol;118(7):1571-83, 1996 Aug. Chang GJ; Wu MH; Wu YC; Su MJ

Resumo: 1. The antiarrhythmic potential and electromechanical effects of liriodenine, an aporphine alkaloid isolated from the plant, Fissistigma glaucescens, were examined. 2. In the Langendorff perfused (with constant pressure) rat heart, at a concentration of 0.3 to 3 microM, liriodenine was able to convert a polymorphic ventricular tachyarrhythmia induced by the ischaemia-reperfusion (EC50 = 0.3 microM). 3. In isolated atrial and ventricular muscle, liriodenine increased the contractile force and slowed the spontaneous beating of the right atrium. 4. The liriodenine-induced positive inotropy was markedly attenuated by a transient outward K+ channel blocker, 4-aminopyridine (4-AP) but was not significantly affected by propranolol, propanolol, verapamil or carbachol. 5. In rat isolated ventricular myocytes, liriodenine prolonged action potential duration and decreased the maximal upstroke velocity of phase 0 depolarization (Vmax) and resting membrane potential in a concentration-dependent manner. The action potential amplitude was not significantly changed. 6. Whole-cell voltage clamp study revealed that liriodenine blocked the Na+ channel (INa) concentration-dependently (IC50 = 0.7 microM) and caused a leftward shift of its steady-state inactivation curve. However, its recovery rate from the inactivated state was not affected. The L-type Ca2+ currents (Ica) were also decreased, but to a lesser degree (IC50 = 2.5 microM, maximal inhibition = 35%). 7. Liriodenine inhibited the 4-AP-sensitive transient outward current (Ito) (IC50 = 2.8 microM) and moderately accelerated its rate of decay. The block of Ito was not associated with changes in the voltage-dependence of the steady-state inactivation curve or in the process of recovery from inactivation of the current. Liriodenine also reduced the amplitude of a slowly inactivating, steady-state outward current (Iss) (IC50 = 1.9 microM). These effects were consistent with its prolonging effect on action potential duration. The inwardly rectifying background K+ current (IK1), was also decreased but to a less degree. 8. Compared to quinidine, liriodenine exerted a stronger degree of block on INa, comparable degree of block on IK1, and lesser extent of block on Ica and Ito. 9. It is concluded that, through inhibition of Na+ and the Ito channel, liriodenine can suppress ventricular arrhythmias induced by myocardial ischaemia reperfusion. The positive inotropic effect can be explained by inhibition of the Ito channel and the subsequent prolongation of action potential duration. These results provide a satisfactory therapeutic potential for the treatment of cardiac arrhythmias.

Panaxadiol

Calcium channel blockade and anti-free-radical actions of panaxadiol saponins Rb1, Rb2, Rb3, Rc, and Rd

Zhongguo Yao Li Xue Bao;16(3):255-60, 1995 May. Zhong GG; Sun CW; Li YY; Qi H; Zhao CY; Jiang Y; Wang XM; Yang SJ; Li H

Resumo: 1-xanthine oxidase 5.3 nmol.L-1, but Rd in the same dose behaved none of the effects. CONCLUSION: Rb1, Rb2, Rb3, and Rc had both probabilities of calcium channels and 30 mumol.L-1 antagonized the increase of free radical content induced by xanthine 0.42 mmol.L-1-xanthine oxidase 5.3 nmol.L-1, but Rd in the same dose behaved none of the effects. CONCLUSION: Rb1, Rb2, Rb3, and Rc had both the calcium channel blockade and anti-free-radical actions.

Agauria salicifolia

The effects of Agauria salicifolia leaf extract on calcium current and excitation-contraction coupling of isolated frog muscle cells.


Resumo: The effects of the ethanolic extract of Agauria salicifolia (AS) previously tested on sodium currents of normal and TTX-treated voltage-clamped skeletal and cardiac muscle cells was investigated on mechanisms involved in the excitation-contraction coupling of the same biological preparations. AS (10(-6) g/l) prolonged the action potential duration whereas the associated contraction was depressed. This is not due to the blocking action of AS on the tubular sodium current since similar results were obtained in the presence of high tetrodotoxin (TTX) concentrations. This is not due to some blocking action of AS on the L-type calcium current since this type of calcium current was enhanced by the extract. In contrast, the cardiac T-type calcium current was decreased by 10(-6) g/l AS. AS exerted a dose-dependent (tested for concentrations ranging from 5 x 10(-10) to 5 x 10(-5) g/l) inhibition of the two components of the contractile response elicited by durable depolarizations, with a prominent effect on the tonic phase. This effect was partially relieved by increasing the external divalent cation (Ca2+ or Cd2+) concentration. At the same concentration it shifted the inactivation/potential relationship for tension by 20 mV towards negative potentials. It is concluded that the inhibitory action of AS on excitation-contraction coupling is partly or completely due to the enhancement of the voltage- and Ca(2+)-dependent inactivation processes of the voltage-sensor.