Canales ionicos farmacologia pdf

Schematic diagram of the ion channel. 1 - channel domains (usually four per channel), 2 - outside the lobby, 3 - selectivity filter, 4 - the diameter of the selective filter, 5 - site phosphorylation, 6 - cell membrane. Ion channels are a type of transmembrane protein that allows certain ions to pass through the cell membrane. Its structure is the same as pores or water-filled canal with a gate system. Its function allows generating action potentials in excitable cells, maintaining internal cell homeostatics, supplying ingredients or conditions necessary for biological functions such as hormone synthesis, mucus production and others. Thus, ion channels are proteins that control the passage of ions through the plasma membrane, such as Naz, CK, Ca2 and Cl, and therefore depend on the electrochemical gradient of each particular ion. In the case of excitable cells such as myocytes and neurons, the gradient of various ions establishes the potential of dormant membranes and activation of certain channels generates the potential for action to perform muscle contractions, release neurotransmitters and regulate genetic expression, among other functions. In the case of unexcitable cells, the ion channels determine the flow of salt and water by regulating the volume of cells and pH. Ion channels are structurally very diverse, but they have common characteristics. They usually act as gates, opening or closing against various stimuli, such as: membrane potential linking neurotransmitters, concentration of certain ions or mechanical forces. Once opened, the flow of different ions can reach 106 or 107 ions per second. They can be particularly selective for certain ions, such as sodium channels, potassium channels and calcium channels; or be non-selective, such as nicotine receptors. The basic description of all living cells must acquire raw materials for biosynthesis and energy production from the environment, and waste should be freed from metabolism. The cells facilitate the exchange of matter with the environment and are surrounded by a plasma membrane that separates their inner part from the outer part. Several polar compounds can dissolve in the lipid bippe and cross the plasma membrane without any obstacles (diffusion of fat-soluble particles such as oxygen, alcohol, fatty acids and others). However, in the case of polar compounds (e.g. sugars, amino acids, ions of ions) membrane protein is essential for transmembrane transport, once The lipid structure of the bive is not easily permeable for this type of particle. These substances are transported to and from the cell or between different intracellular compartments by membrane proteins such as pumps, conveyors and ion channels. Ion channels are made up of glycoproteins and are important components in the activity of all cells. The channels have three important properties: they control ion; Recognize and select ions (channels can be selectively permeable to one or more ions); open and close in response to electrical, chemical or mechanical stimuli. Ion channels form membrane pores that can be opened and closed. When the ion channel opens, it forms an aqueous pore that extends through the thickness of the membrane. The flow of ions through the canal due to differences in electrical potential or concentrations is passive, i.e. does not require energy expenditure on the metabolism of the cell. The ions flow passively in favor of its electrochemical gradient. Energy comes from chemical forces diffusion, mosis and electrochemical balance. Thus, the two great forces that control the ions move the difference in concentration and the electric gradient (both called electrothic force). Since the region with the highest concentration is more likely to collide particles with each other, the migration of particles from this region to a lower concentration is thermodynamically favored, the particle is said to move in favor of a chemical gradient or concentration. Ion channels can be of two types: filtering - they are always open; gates - they open and close in response to some kind of stimulus. Mechanisms for opening or closing ion channels In electrophysiology, the English term gating is often used to refer to discovery (through activation) and closure (through deactivation or inactivation) of ion channels. The name gating (from the gate, door, gate) comes from the idea that the protein of the ion channels includes pores that are protected by one or more gates, and the gate (s) must be open to ions to pass through the pores. Various cellular changes can cause the activation of the gate (s), depending on the type of ion channel concerned, among other things: changes in tension in the cell membrane (tension of activated ion channels), chemicals (drugs, addictive substances, hormones) that interact with the ion channel (ligand-activated ion channels), temperature changes, cell membrane, the addition of a phosphate group to the ion channel (phosphorylation) and interaction with other molecules in the cell (e.g. G-proteins). The rate at which any of these activation/inactivation processes occurs in response to these stimuli is known as kinetic activation. Some drugs and many toxins act as modifiers of activation of ion channels by changing the kinetics of the gate. Some channels open or close randomly, regardless of the cost of membrane potential and your gating is said to strain independently. In contrast, other channels are usually closed, but their chances of opening can be significantly increased by changing the membrane potential (stress-sensitive ion channels); specific interactions with extracellular or intracellular ligatures (ligature channels); or physical stimuli (mechanrectors and heat-sensitive channels). When the ion channels are closed (there is no possibility of holding), they are ion-impenetrable and do not conduct electric current. When the ion channels are opened, they control the electric current and then allow some ions to pass through them and therefore through the cell's plasma membrane. These ion streams generate an electric current through the membrane. The direction in which they move, as mentioned above, is determined by an electrochemical gradient, which represents the amount of the chemical gradient through the plasma membrane and the electric field experienced by the ion. Activation is the process in which the ion channel is transformed and moved from any of its driving states to any of its restless states. The usual description of voltage-activated ion channels of action speaks of four processes: activation, deactivation, inactivation, and reactivation (also called inactivation recovery). In the model of ion channels with two gates (gate activation and gate inactivation), in which both must be opened to ions to be controlled through the channel, activation is the process of opening the activation gate, which occurs in response to the fact that the voltage in the cell membrane (membrane potential) becomes more positive in relation to the outer side of the cell (depolarization); deactivation is the opposite process, i.e. closing the gate in response to the fact that the voltage inside the membrane becomes more negative (repolarization. Inactivation is the closing of the inactivation gate; as with inactivation occurs in response to the fact that the voltage inside the membrane becomes more positive, but often occurs with a delay, compared to activation. Recovery after inactivation is the opposite of inactivation. Thus, both inactivation and deactivation are processes that cause the canal to lose its ability to conductivity, but are different processes in the sense that inactivation is triggered when the inner part of the membrane becomes more positive, while deactivation is triggered when the membrane potential becomes more negative. Ion channels can be categorized according to the type of stimulus to open or close: voltage-activated channels; Ligando-activated channels; mechanal frozen channels. The voltage-regulated channels of the Ion Channel, adjustable by voltage, reveal the difference in transmembrane potential and is selective for a certain type of ions, as pores are polarized and have a size similar to the ion. Ion channels open up in response to changes in electrical capacity through the plasma membrane, which is usually a lipid bipa. Its main function is the transmission of electrical impulses (generating action potential) due to changes in the difference in electrical loads derived from concentrations of anions and cats between both sides of the membrane. The probability of closing and opening ion channels is controlled by a sensor that can be electrical, chemical or mechanical. Voltage-activated channels contain a sensor that includes several positively charged amino acids that move into the electric membrane field during the opening or closing of the channel. Changing the difference in electrical potential on both sides of the membrane leads to the movement of the sensor. The movement of the voltage sensor creates a load movement (the so-called gate current), which changes the free energy that changes the tertiary structure of the channel, opening or closing it. Some of these channels have a fire-resistant state known as inactivation, the mechanism of which is provided by a unit independent of those responsible for opening and closing. Sodium Channels (NAH) Phase of rapid depolarization of the action potential of nerve and muscle cells (skeletal, smooth and cardiac) and, in general, excitable cells, depends on the entry of Naz through channels activated by voltage changes. This Naz input depolarizes the membrane potential, which in turn facilitates the discovery of more Naz channels and allows to achieve the equilibrium potential of this ion at the level of 1-2 msek. When cells are at ease, the probability of opening Channels Na very low, although during depolarization this leads to a sharp increase in the probability of its discovery. The channels of potassium (CK) of CK are the most heterogeneous group of membrane structural proteins. In excitable cells, cell depolarization activates the channels of the C.P. and facilitates the exit of the CK from the cell, which leads to the repolarization of the membrane potential. In addition, CK channels play an important role in maintaining the potential of cellular rest, frequency of firing of automatic cells, release of neurotransmitters, insulin secretion, cellular excitability, transporting electrolytes through epithelial cells, reducing smooth regulation of muscle mass and cell volume. There are also CK channels, the activation of which does not depend on changes in membrane potential, which determine the potential of rest and regulate excitability and extracellular volume. Vinegar Fly (Drosophila melanogaster) was the key that allowed us to know the topology and function of the CK channels. The identification of the first channel of CP was the result of an electrophysiological study of the mutant Shaker D. Melanogaster, named because he has spasmoscopic movements of the limbs during anesthesia ether. An important function of the CK channels is the activation of lymphocytes in the body's immune response. Calcium channels (Ca2) In rest cells, the intracellular concentration of Ca2 is 20,000 times lower than its concentration in extracellular environment; On the other hand, the cellular interior is electronlegative (-50 to -60 mV), that is, there is an electrochemical gradient that promotes the entry of Ca2 ions into the cell. However, in the resting cell, the cell membrane is very little permeable to Ca2, so the cell's input in favor of this gradient decreases. However, during cellular activation, Ca2's intracellular concentration increases as a result of entering extracellular Ca2 through the membrane or through voltage-dependent channels. The entry of Ca2 through the voltage-dependent channels of the cell membrane is involved in the regulation of numerous biological processes: genesis of action potential and duration of this, arousal-reduction of communication, release of neurotransmitters, hormones and growth factors, synaptogenesis, osteogenesis, cell differentiation processes, hypertrophy and remodeling, among others. Chloride (Cl_) is a human-1 chloride channel (Cl C-1), inside the cell membrane. Cl-channels play a very important role in regulating cellular excitability, transepitional transport and volume and pH regulation and can be activated by changes in voltage, endogenous ligaments (Ca, AMPc, G proteins) and physical forces (cell enlargement). The first voltage-dependent channel in this family, called CLC-0 (Cl C-0), was cloned from the electric organ of the Marmorata Torpedo band. Subsequently, 9 more channels encoded by the genes CLCN1-7, CLCNKa and CLCNKb. Channels Cl C-0, Cl C-1, ClC-2 and ClC-Ka/b are located in the cell membrane, and the remaining channels are located in the membranes of mitochondria and other cellular organelles. The channels located in the cell membrane stabilize the membrane potential in excitable cells, as in skeletal muscles, and are responsible for the transept transport of water and electrolytes, while intracellular channels can balance the current produced by the proton pump. The Cl C-1 chlorine channel is crucial for the excitability of skeletal muscles, stabilizing the membrane potential of myocytes. The most important function of cl-channels, in neural synapses, is to cause hyperpolarization by its entrance to the post-synaptic neuron after activation, and thus interrupt the nerve impulse to prepare the post-synaptic neuron for the next impulse. Another important function of Cl-channels occurs in red blood cells: in the tissues the input of Cl- into red blood cells causes bicarbonate to exit them, injecting CO2 into red blood cell. In the lungs, the release of Cl- from red blood cell causes bicarbonate from the blood to enter, leaving CO2 in the pulmonary blood. It is transported more CO2 from tissues to the lungs. Channels regulated by ligands of ion channels are opened in response to the binding of certain neurotransmitters or other molecules. This opening mechanism is associated with the interaction of a chemical (neurotransmitter or hormone) with a part of the channel called a receptor, which creates a change in free energy and alters the conformation of the protein, opening the channel. Ligandos regulate the opening of receiver channels. These channels are called dependent ligates and are important in synaptic transmission. Dependent ligating channels have two mechanisms of discovery: by binding the neurotransmitter to the receptor associated with the channel (ionotropic receptors, directly activated receptors); binding a neurotransmitter to a receptor that is not connected to the channel. This causes a cascade of enzyme phenomena as soon as the activation of protein G contributes to the opening of the channel due to the action of phosphorylation enzymes. In the case of activated ligando channels, the sensor is an area of the protein channel, exposed either from the outside or inside the membrane, which connects to a large affinity of a particular molecule, leading to the opening or closing of the channel. Mechanical channels, adjustable by mechanical impulse, open in response to mechanical action. Mechanical channels, such as those found in the Pacini corpuscles, are open stretching the cell membrane in conditions of pressure and/or tension. The mechanism of the sensor in the last type of channels is not yet clear, however, it has been suggested that the fatty acids of the membrane act as sensory agents by activating phospholipsase attached to the membrane1, or it has been suggested that the cytoskkel, which is directly under the channel, is involved. The biological role of ion channels is especially important in transmitting electrical impulse to the nervous system. In fact, most of the toxins that some organisms have developed to paralyze the nervous system of predators or prey (such as poison-producing scorpions, spiders, snakes and others) work by clogging ion channels. The high affinity and specificity of these toxins allowed them to be used as ligands to purify the proteins that make up the ion channels. Many therapeutic agents mediate their effect by interacting with these proteins such as some anxiolytic, antihypertensive, anti-arthythmic agents, etc. ion channels occur in a wide variety of biological processes that require rapid changes in cells such as the heart, skeleton, muscle contraction, transporting ions and nutrients through epithelials, activation of cells or the release of cells. Ion channels are a key goal in the search for new drugs. Properties of ion channels related to their function - transporting ions through these channels is very fast. More than one million ions per second can flow through them (107-108 ions/s.) Flow a thousand times faster than the speed of protein transportation, so ion transport is quite effective. - High selectivity. Ion channels are selective from the types of ions that allow them to cross. The type of ion you can pass depends on the electrochemical configuration of the protein divisions, especially on the underside of the pore: usually the type of ion channel allows you to pass several types of ions, especially if they have the same load (positive or negative). In some cases, its opening and closure may be regulated in response to specific incentives. Related diseases Ion channels (canalopathy) The importance of ion channels in physiological processes is evident from the effect of mutations on specific proteins of ion channels. Genetic defects in the voltage-controlled gates of the Na' plasma membrane myocytes lead to diseases in which muscles are periodically paralyzed (as in hypercaemic periodic paralysis) or become rigid (as in congenital paramyotonia). Cystic fibrosis is the result of a mutation that alters the amino acid in the cfTR protein, the Cl-ion canal; here the faulty process is not neurotransmission, but the secretion of several exocrine glandular cells whose activity is associated with Cl-ion flows. Many toxins present in nature often act on ion channels, and the potency of these toxins once again illustrates the importance of the normal functioning of ion channels. Tetradotoxin (produced by puffet fish, Sphaeroides rubripes) and saxitoxin (produced by marine dinoflagelat Gonyaulax, which causes red tides) act by joining the voltage regulated gates of na' channels of neurons, themselves normal action potentials. Puffer fish is an ingredient of the Japanese fugu delicacy, which can only be prepared by chefs specially trained to separate such a juicy bite from the deadly poison. Eating seafood that is fed Gonyaulax can also be fatal; Seafood is not sensitive to saxytoxin, but they concentrate it on its muscles, which become very poisonous to organisms higher in the food chain. The poison of the black snake mamba contains arboretum toxin, which interferes with the voltage-adjusted input channels of the CK. Tubocurarine, an active ingredient in curare (used as a poison for arrows in the Amazon) and two other toxins of snake venom, cobrotoxin and bungarotoxin, block the acetylcholine receptor or prevent the discovery of its ion channel. By blocking signals from nerves to muscles, all these toxins cause paralysis and, most likely, death. On the positive side, the extremely high affinity of bungarotoxin for the acetylcholine receptor was experimentally beneficial: a radioactively marked toxin was used to quantify the receptor during cleaning. In recent years, various congenital diseases have been reported related to mutations in genes coded by the ion canal division, canal feeds. Using molecular biology and electrophysiological methods, genes that encode ion canal units and homes or mutated channels. Today we know that mutations of the channels Na, Ca2, K and Cl- are responsible, in particular, for images of epilepsy, ataxia, degeneration of neurons. Patch-clip method Main article: Patch clamp using this ion current technique can be measured through a separate membrane channel. To do this, the capillary is connected to a modified thin tip with a diameter of 1 mm on the cell membrane; a small vacuum places a dense cell membrane on the edge of the glass and thus insulates a small membrane domain (patch) from the environment. Mechanical manipulation can separate the fragments of the cell membrane and then measure them individually. The electrode in the buffer-filled capillary is sufficient to connect the measuring devices. If a certain potential is fulfilled (for the clamp, staple) the ion current can be measured through an isolated high-resolution membrane domain (s). For this condition the cytosolized side (outside) or extracellular side of the membrane (inside) can be arbitrarily varied and measure its effect on the ion current. This is quantitatively ion current through the nicotine receptor acetylcholine about 4 pH (10-12 amps), which means a flow of about 2-3 x 104 Naz ions per millisecond. The history of the ion canal concept was proposed in the 1950s by Alan Hodgkin and Andrew Huxley in their classic research on the nature of nerve impulse in the giant squid axon. In their quantitative model, they hypothesized that the currents of Naz and CK are located in certain locations of the membrane, which they call active spots. We now know that these active patches are the voltage of the activated CHANNELS NA and 3K. Since then and over the past 50 years, knowledge of ion channels has increased significantly at the molecular level. A breakthrough in the knowledge of ion channels was also given with the development of the technique of patch clamp Erwin and Bert Sackmann. The two researchers used a glass microelectrode with its polished tip and applied it to the cell surface so that a small membrane patch could be isolated. The tension through this patch remained stable thanks to the feedback amplifier, and thus they were able to measure the currents flowing through the channels present in it. Another breakthrough was made in the study of the ion channels that brought the Nobel Prize to its authors. Roderick McKinnon's group managed to crystallize the ion channel for the first time and study it with X-ray diffraction by obtaining 3.2o images. Ion Channel in The Plastic Art Birth of An Idea (2007) by Julian Voss-Andrea. The sculpture was commissioned by Roderick McKinnon and represents the atomic coordinates of a molecule determined by the McKinnon Group in 2001. Roderick McKinnon has commissioned artist Birth Ideas, a 1.5-metre

sculpture inspired by the kcsA potash channel. The work consists of a wire object representing the inside of the canal and another blown glass, representing, in turn, the main cavity of the canal structure. Watch also the Calcium Channel sodium channel nicotine receptor Dr. Erwin Nobel Prize in Physiology 1991 Dr. Bert Sackman Nobel Prize in Physiology 1991 Nobel Prize in Physiology and Medicine bibliography neurology (II edition) Dale Purves, George J. Augustine, David Fitzpatrick, Lawrence. C. Katz, Anthony-Samuel Lanatia, James O. McNamara, S. Mark Williams, editing by S. Mark Williams, Editing by Mark Williams Published by Sinauer Associates, Inc. (2001) online texts Major Neurohimy: Molecular, Cellular and Medical Aspects (VI Edition) George J Siegel, Bernard W Agranoff, RV Albers, Stephen K Fisher and Michael D Uhler published by Lippincott, Williams and Wilkins (1999): texts online Neverisky Links, Daniel L.; Abbott, Jeffrey W. (July to August 2015). Ion channel-transporter interactions. Crete Rev Biochem Mole Biol 51 (4): 257-267. PMID 27098917. doi:10.3109/10409238.2016.1172553. Received on February 25, 2018. Skerratt, Sarah E.; West, Christopher W. (November to December 2015). Ionic channel therapy for pain. Channels (Austin) (Taylor and Francis) 9 (6): 344-351. PMID 26218246. doi:10.1080/19336950.2015.1075105. Received on February 25, 2018. b Subramaniam, Prakash; Colcraft, Henry M. (January 2015). Ion Canal Engineering: Perspectives and Strategies. J Mole Biol 427 (2): 190-204. PMID 25205552. doi:10.1016/j.jmb.2014.09.001. Received on February 25, 2018. Martinez Rosas, Martin (April to June 2004). Ion channels: biology and pathology. Archives of Cardiology of Mexico (Mexico: National Institute of Cardiology Ignacio Chavez) 74 (supl. 2): S205-S210. Received on February 25, 2018. Alberts, Bruce; Dennis Bray; Julian Lewis; Martin Raff; Keith Roberts; Watson D. (1994). Molecular cell biology. New York: Garland. 523-547. ISBN 0-8153-1620-8. Cesare, Morioondo A, Vellani V, McNaughton PA (1999). Ion canals closed by heat. Proc. It's thlat. Akkad. Sci. United States, 96 (14), July, 7658-7663, PMID-10393876, PMC-33597, DOI-10.1073/pnas.96.14.7658, . Hill, B. (2001). Ion channels of excitable membranes. Sunderland, Massachusetts: Sinauer. ISBN 0-87893-321-2. M. Berg, Jeremy; Luber Strier (2003). Biochemistry (5th edition). Come back. ISBN 10 8429174849 'isbn' wrong (help). Alfonso Vega Hernandez; Ricardo Felix (March-April 2001). 'Physiopathology of stress-sensitive ion channels' (pdf). 96. Received in 2009. (Broken link is available in the internet archive; see the history and the latest version). Wang K, Preisler SS, Chang L, Cui Y, Missel JW, Grunberg C, et al (2019). Human chloride structure ClC-1. PLoS Biol 17 (4): e3000218. Received on May 11, 2019. Lozano, J.A.; J.D. Galindo Kazakov (2000). Biochemistry and Molecular Biology for Medical Sciences (2nd edition). McGraw Hill. ISBN 9788448602925. The help uses an outdated parameter of co-authors (help) - Werner Mueller, Sterle (2008). Biochemistry, Basics of Medicine and Life Sciences (1st edition). Come back. ISBN 978 84 291 7393 2. Pathology of ion channels: canalopathy (pdf). page 108. Archive from the original on November 10, 2007. Received in 2009. Nelson, D.L.; M.M. Cox (2004). Lehninger Principles of Biochemistry (4th edition). WTT Freeman. ISBN 0 7167 4339 6. The help uses an outdated co-author option (help) - Ball, Philip (March 2008). The crucible: Art inspired by science must be more than just a beautiful painting. World Chemistry 5 (3): 42-43. Received on January 12, 2009. External Links Spanish Federation of Cystic Fibrosis Distribution action potential data: No. 62536 Multimedia: Ion channels received from canales ionicos farmacologia pdf. receptores asociados a canales ionicos farmacologia. receptores de canales ionicos farmacologia. farmacologia de los canales ionicos. que son los canales ionicos en farmacologia