SANITAS MAGISTERIUM

Received: February 1, 2018
Revision Received: February 1, 2018
Accepted: February 15, 2018
OnlineFirst: March 1, 2018

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Lavender Phytopreprate for Local Analgesia Through Healthy or Damaged Skin

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Abstract

The purpose of this research is the creation and experimental study of a new locally-anesthetized aromotherapeutic phytoprotect "LMKsolutio" for analgesia through healthy or damaged skin. As a simple and objectively measurable and tamper-resistant local pain stimulus, we used a straight-line low-voltage electrical current with standardized parameters, from a "Galvanostat" device, giving 0 to 50 mA. When applied by spreading or spraying without dressings on healthy or damaged skin of the "LMKsolutio" at a dose of 0.02ml / cm2, the increase in the threshold of irritability (sensitivity) as an objective indicator for somatic (skin and mucous membrane) analgesia and deep somatic (in the muscles, tendons, periosteum or joint capsules) pain is a rapid onset (3-5 minutes), between 15 and 40 minutes the irritability threshold is 18 - 36 - 44 times higher and up to 50 minutes is kept up to 12-20 times higher. After 24-48 hours, a slight transient local allergic reaction to the Lavender oil that can be prevented by premedication is possible.

Keywords:
Analgesia, Aromatherapy, Phytopreparate, Skin

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Citation: Pirovski, T.H. & Stayko, Y. (2018). Lavender Pyhtoreprate for Local Analgesia Through Healthy of Dmaged Skin. Sanitas Magisterium, 3(2), 40-46.

Pain is "an unpleasant sensory and/or emotional experience associated with actual or potential tissue damage or an inconvenient condition described by the terms of this disability" (Атанасов et al., 2007). In a medical aspect, pain is a subjective expression of the action of stimuli, which by force, site of action and interaction are capable of damaging the tissues and/or bringing into the body a nociceptive defense Response (Olapour. et al., 2013) Pain is characterized as somatic (in skin and mucous membranes), deeply somatic (in muscles, tendons, periosteum or joint capsules) and visceral (in the internal organs) (Ochroch & Gottschalk, 2005).Pain sensing sensors are the terminal free nerve endings of the sensory nerve fiber – noci sensors associated with thin myelin or non-myelin fibers in sensory modules(Pritchard, 2009). Their density is higher in the skin and subcutaneous tissue, ligaments, fascias, joint capsules of vascular adventitia and parietal sheets of the pleura and peritoneum.

Mechanisms for the conversion of pain stimuli into receptor potential are accomplished by a sensor complex composed of a receptor coupled to one or more ion channels that generate depolarizing currents or events in response to the stimulus. Three different receptor transducers are described - mechanical (for deformation, stretching, compression), thermal (over 42^0C) and chemical (ions, salts, metabolites, etc.). The ion channels in the sensor complex are Ca2 + or Na +. Their functional capabilities, the ion flow, is determined by the channel flow rate, the duration of its active open state and its mobility, as well as the number of effluent channels in the membrane(Alaoui et al., 2017). When changing the polarity of the nerve membrane as a result of the passage of Na + and K + ions through the respective channels using a K + / Na + pump, local anesthetics inhibit Na + invasion and depolarization of the membrane by acting on the Na + channel(Schuwald et al, 2013). This brief feature of somatic and deeply somatic pain shows the importance and possible mechanisms of suppression by local anesthetics for the symptomatic treatment of minor traumas and injuries (sprains, bruises, edema); in environmental stressors with destructive effects on tissues (mechanical, physical, chemical, biological); in small surgical interventions; as well as to prevent the malignant modification of the nervous system and the possible breakdown of the vital functions of the body from the powerful distress action of the pain (van Wyk., 2008)

The advantages of local anesthetics in their use are that their anesthetic effect can be enhanced by combining them with other drugs and excipients. In addition, their use reduces the risk of the anesthetic preparation falling into the bloodstream, which is an advantage as it is possible to modify the pharmacodynamics and pharmacokinetics of both the anesthetics themselves and their interacting substances (Слюсарь, 1982).

The disadvantage of local anesthesia through undamaged or damaged skin, however, is associated with side effects, a small therapeutic latitude and systemic toxicity of the anesthetics so far used for this purpose, which, as conditions necessary for their passage through the lipophilic keratin layer of the skin and providing the action in an aqueous medium, a high concentration in the form of a lipophilic base and a high degree of ionization at physiological pH is required at the same time.

It is known (Прянишникова et al., 1969) that while the non-ionized form (base) is responsible for penetrating the anesthetic through the skin and the myelin envelope of the nerve to the site of action, its cationic form interacts with receptors in the nerve membrane. That is, the biopharmaceutical aspects (МинковЕвг et al., 1994) of Biologically Active Substances (BAS)-anesthetic dermal medications are particularly important for the penetration of BAS in the stratum corneum and the deeper layers of the epidermis of the skin and for the permeation of BAS through the skin and the possibility of percutaneous absorption(Olapour. et al., 2013).

Of the properties of BAS, their solubility (M/B), the distribution coefficient (water/skin) and the diffusion coefficient are of utmost importance. Transdermal resorption of BAS is enhanced by vasodilation, mechanical massage, including massage phyto products (through the hair follicles and sebaceous glands) and the postperpirational ability of the sweat glands, which, after activation and end of sweat, induce BAS solutions in contact with the skin.

Purpose

The aim of the current scientific and applied research is the creation and experimental study of new locally-anesthetizing aromatherapeutic phytoprotect "LMKsolutio" for analgesia through healthy or injured (traumas, cold, burns, etc.) skin in somatic (in skin and mucous membranes) and deep somatic (in the muscles, tendons, periosteum or joint capsules) pain

Method

For the experimental study of the strength and duration of the action of such a preparation, applied on a healthy skin and without occlusion afterwards, it is important to note that today it is still not possible to measure objectively the force of pain as a sensory component and as an unpleasant emotional and psychosocial reaction " (Атанасов et al., 2007). Therefore, we have decided to use as an easily and objectively measurable and tamper-resistant local pain stimulus - a straight-line, low-voltage electrical current with standardized parameters supplied by electrodes with standard desiccated wet water cushions from a Galvanostat apparatus giving 0 to 50 mA of electrical current (*Рязкова & Кирова, 2002)* . Initially, three times the individual threshold of irritation (sensitivity) about that current at a given time and place on the skin of the same person (for example, a positive electrode from the inside of the left arm or right arm, and negative - on the outside), taking into account the values of the power of the "Galvanosta" current, causing an initial sensation of irritation. After 30 minutes, a healthy skin is smeared (sprayed) on an area of 50 cm2 at the test place with "LMKsolutio" at a dose of 0.02 ml / cm2 (i.e., 1 ml). After 2 minutes during which the phyto product "absorbs", the positive electrode (anode) from the inside of the forearm and the negative (the cathode) from the outside are placed and the "Galvanostat" is switched on. From the 3rd minute to the 60th minute every minute the "Galvanostat" is turned on and off and we note the value of the incrementally increased by us 1 mA current strength (from 0 to 27 mA), which again leads to the same initial sensation of irritation ("biting").

With respect to the time-force dependence data, constant and standardized other parameters are plotted as graphical expression of the change in the threshold of irritability (sensitivity), an objective indicator of the strength and duration of the anesthetic action of the preparation.

The new locally-anesthetizing aromatherapy phytoprotect "LMKsolutio" for analgesia through healthy or injured (traumas, cold, burns, etc.) skin in somatic (in skin and mucous membranes) and deeply somatic (in muscles, tendons, periosteum or joint capsules), investigated by this method, is a suitably constructed by us composition with a predetermined mechanism of action that prevents the generation and administration of the receptor potential from pain irritants in the nerve endings manifested in the change of the threshold sensitivity, containing in certain ratios:

Ethereal Lavender Oil (EPO Monograph 1338), Carbamide, Diethylether, Ethanol, Distilled Water,
and Non-ionic Mixed Surfactant (PVA) with an Appropriate HLP value

Results and Discussion

Urea O = C- (NH2) 2 has a keratolytic effect - dissolves hydrophobic compounds and is inserted between keratin molecules, where keratin is dispersed and softened, which greatly facilitates the penetration of substances through the skin (Scheinfeld, 2010; Loden, 2005).

Furthermore, urea is a chaotropic agent - a solubilizer which increases the water solubility of the non-polar groups of substances and acts along with the added nonionic surfactant. With prolonged stay in dilute aqueous solutions and in cold, from urea, active cyanate ions (NCO-) are produced capable of binding H + and cations (Ca 2+ as calcium cyanamide) (Машковский., 1974; Dawson et all., 1986)

Diethylether and Ethanol, as well as solvents and activators of resorption (Грецкий & Цагарейшвили, 1979) , also act by locally lowering the temperature of the skin by rapid evaporation of the skin causing it to contract blood vessels, which reduces the risk of anesthetics in the blood. and then evaporation, the local concentration on the skin of the dissolved in them and in the water substances, increases and changes the distribution coefficient (water/oil/skin) and their diffusion coefficient through the skin, which together with non-ionic mixed surfactant with an appropriate HLP value, improves the permeation (passage) of BAS through the skin and the possibility of their percutaneous absorption (Smith, 2009).

Lavender oil contains 27 components, some of which are: 0.8% alpha and beta pinen; 13% terpineol-4; 5% cinnol; 30-50% (19-36-47% in the Bulgarian oil) linoleacetate; camphan; miercen; lemon; amylvinylcarbinol; 25-45% (28% in the Bulgarian oil) aliphatic monoterpene - free linalool; borneol; geranyl acetate and others (Koulivand et al., 2013; Cavanagh & Wilkinson, 2012). It, through deep penetration and solubility in the lipids under the skin, after initial stimulation (irritation and redness) of the skin causes quite strong anesthesia (Woronuk et al., 2011). Lavender oil (based mostly on pine, terpineol, cyneol, and the linoleic acid containing carboxyl oxygen in the molecule), unlike any other essential oils - antioxidants, has a pro-oxidant activity (electron acceptor) that accept electrons and becomes reduced (Petrovska, 2012) .This property is particularly important in our opinion because of its anesthetic ability associated with ionic asymmetry, due to electron attraction and capture during its reduction which prevents membrane depolarization and the formation of the Na + cationic action potential, as well as the change in ionic permeability in the sensor complex by influencing the surface tension of the phospholipids of the axon biomembrane from the neutral (reduced) form of the Lavender oil (Alaoui et al., 2017).

In addition, Lavender oil has a broad antimicrobial spectrum (Bakhtshirin et al., 2015) (yeast sponges, bacteria, primers) and accelerates repair processes in damaged skin, especially in traumas and burns, and is also low in toxicity (LD50 = 0.17 g)

The charts for a two-fold experimental study of the change in the threshold of irritation (sensitivity) of healthy human skin in the event of an electric shock with force in mA, in time in minutes, after coating or spraying with "LMKsolutio" at a dose of 0.02 ml/cm^2 at an initial irritancy threshold of 0.6 mA and 1.4 mA respectively of the same person over a 16 day interval, can be seen in Figures 1 and 2.

Figure 1
Right hand

Figure 2
Left hand

Conclusions

When applied by spreading or spraying without dressings on healthy or damaged skin of the "LMKsolutio" at a dose of 0.02ml /cm^2, the increase in the threshold of irritability (sensitivity) as an objective indicator for somatic (skin and mucous membrane) analgesia and deep somatic (in muscles, tendons, periosteum or joint capsules) pain is of a rapid onset (3-5 minutes), between 15 and 40 minutes the threshold of irritability is 18 - 36 - 44 times higher and up to 50 minutes is kept up to 12-20 times higher. After 24-48 hours, a slight transient local allergic reaction to the Lavender oil that can be prevented by premedication is possible.

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