



HU000025775T2

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Szellemi Tulajdon Nemzeti Hivatala(11) Lajstromszám: **E 025 775**(13) **T2****EURÓPAI SZABADALOM**
SZÖVEGÉNEK FORDÍTÁSA(21) Magyar ügyszám: **E 09 776551**(22) A bejelentés napja: **2009. 04. 22.**

(96) Az európai bejelentés bejelentési száma:

EP 20090776551

(97) Az európai bejelentés közzétételi adatai:

EP 2293805 A2 **2010. 01. 14.**

(97) Az európai szabadalom megadásának meghirdetési adatai:

EP 2293805 B1 **2015. 07. 29.**(51) Int. Cl.: **A61K 361/85** (2006.01)**A61K 36/09** (2006.01)**A61K 363/28** (2006.01)**A61K 36/45** (2006.01)**A61K 36/48** (2006.01)**A61K 36/49** (2006.01)**A61K 36/53** (2006.01)**A61K 365/37** (2006.01)**A61K 36/61** (2006.01)**A61K 36/68** (2006.01)**A61K 36/73** (2006.01)**A61K 367/36** (2006.01)**A61K 367/39** (2006.01)**A61P 11/00** (2006.01)

(86) A nemzetközi (PCT) bejelentési szám:

PCT/EP 09/002913

(87) A nemzetközi közzétételi szám:

WO 10003472

(30) Elsőbbségi adatok:

202008008532 U **2008. 06. 30.** **DE**

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Torok cukorka kompozíció a száj és a garat gyulladáisos betegségeinek kezelésére

Az európai szabadalom ellen, megadásának az Európai Szabadalmi Közlönyben való meghirdetésétől számított kilenc hónapon belül, felszólalást lehet benyújtani az Európai Szabadalmi Hivatalnál. (Európai Szabadalmi Egyezmény 99. cikk(1))

A fordítást a szabadalmas az 1995. évi XXXIII. törvény 84/H. §-a szerint nyújtotta be. A fordítás tartalmi helyességét a Szellemi Tulajdon Nemzeti Hivatala nem vizsgálta.

Lozenge composition for treating inflammatory diseases of the mouth and pharynx

Description

The present invention relates to the field of inflammatory diseases of the mouth and throat area, for example, as a concomitant of colds, as well as cough and catarrhs of the upper respiratory system.

In particular, the present invention relates to a pharmaceutical composition in particular, in a dosage form suitable for sucking, in particular as a lozenge, wherein the composition contains at least a first active ingredient component, containing at least one tanning agent drug, or the extract thereof, respectively, having at least a second active ingredient component, comprising at least one mucilage drug, or the extract thereof, respectively.

Furthermore, the present invention relates to a packaging unit, containing the composition according to the invention in a form suitable for individual dosing, preferably in the form of lozenges.

Furthermore, the present invention relates to the use of the composition according to the invention for the topical treatment of inflammatory diseases of the mouth and throat area, cough and catarrhs of the upper respiratory system, or the production of a drug for the topical treatment of inflammatory diseases of the mouth and throat area, cough and catarrh of the upper respiratory system.

Inflammatory diseases of the mouth and throat area, i.e. inflammation in the area of the oral cavity, and of the throat area, often occur as concomitant of colds and the flu, but also as autonomous diseases. Such inflammatory processes of the mouth and throat area are often accompanied in an affected patient with unpleasant pain symptoms. Non-limiting examples for such inflammatory diseases of the throat area are sore throat, in particular angina, inflammation of the larynx (laryngitis), inflammation of the mucous membrane of the throat (pharyngitis), and inflammation of the tonsils of the throat (tonsillitis). Such diseases of the throat area are often accompanied by difficulties swallowing. Inflammation in the area of the oral cavity, such as stomatitis, gingivitis, oral mucous membrane lesions, and the like, also often present unpleasant symptoms for those affected. For further details on the diseases mentioned above, reference may be made, for example, to the Roche Dictionary of Medicine, 3rd edition, 1993, Urban & Schwarzenberg, Munich/Vienna, Baltimore, as well as to Pschyrembel, Medical Dictionary, 257th edition, 1993, Nikol Verlagsgesellschaft mbH, Hamburg. The term "inflammatory diseases of the mouth and throat area" is therefore meant in a broad sense, and comprises all inflammatory diseases which may occur in the area of the oral cavity and the throat area.

The treatment of inflammatory diseases of the mouth and throat area is accomplished -- as a function of the severity of the disease pattern -- in general by means of a topical and optionally additional systemic therapy, in severe cases. While systemic antibiotics are administered in severe cases, antiseptics and anti-inflammatory agents (e.g. antiphlogistics, agents acting in an anti-inflammatory manner, local antibiotics, etc.) are utilized in support, and in the less severe cases, possibly alone for the topical, symptomatic treatment, which may be administered, for example, in the form of throat rinses, sprays, or lozenges.

The active agent for the topical treatment of inflammatory processes of the mouth and throat area proven particularly successful is 1-hexadecyl Pyridinium chloride (international non-proprietary name: "Cetylpyridinium Chloride (CPC). The same is a quaternary ammonium compound having a bactericidal and fungicidal effect, which are utilized, inter alia, in lozenges. One disadvantage of this active ingredient, however, is the fact that with a high dosage and excessive consumption, gastric and abdominal disorders, shortness of breath, as well as an increased formation of methemoglobin, in particular in children, may occur.

Furthermore, another topical antiseptic, or disinfectant, respectively, which has proven successful for the mucous membrane of the mouth and throat is 1,3-Bis(2-ethyl hexyl)-hexahydro-5-methyl-5-pyridinamine (international non-proprietary name: "Hexetidil"), which

may be applied, for example, as a spray, or in the form of rinsing or gargling solutions. With long-term application and strong dosing, however, it may also cause gastric and abdominal disorders, as well as taste irritation.

Furthermore, active ingredients of natural origin are used, such as e.g. so-called mucilage drugs, or the extracts thereof, such as Icelandic moss (*Lichen islandicus*). These active ingredients are often utilized within the scope of mono-preparations. In this case it is primarily intended to provide the active ingredient in a solid form suitable for sucking, e.g. in the form of a solid lozenge. Such preparations, however, do not always provide the desired therapeutic success.

EP 1 829 548 A1 relates to the use of extracts of the Pelargonium type in combination with plantain extract for the topical prophylaxis or treatment. In particular, the treatment may be in the form of lozenges for the topical treatment of mouth and throat inflammation, or as a cream for the topical treatment of skin disorders.

EP 0 870 507 A1 relates to an antibacterial composition, which is said to contain an herb extract and an essential oil in a defined ratio. The essential oil is said to contain an antimicrobial effect, whereas the herb extract, or the extract from plant materials, is said to have a significantly lower, or even no antimicrobial effect. Special blends of both components are said to develop an antimicrobial effect, which significantly surpasses that of its individual components by far.

GB 2 093 896 A relates to a composition that is suitable for the treatment of hair and/or skin. The composition contains pulverized flowers or flower petals in an aqueous medium, having a particle size of not more than 125 μm in the presence of an adhesive, which aids in maintaining homogeneity of the composition. The adhesive is a thickener, and/or a water-in-oil or an oil-in-water emulsion.

The present invention is therefore based on the task of providing, in particular, a pharmaceutical composition suitable for the efficient topical treatment of inflammatory diseases of the mouth and throat area (i.e. also of inflammatory diseases of the throat and mouth cavity), as well as cough and catarrh of the upper respiratory system, and, in particular, is to at least essentially avoid, or at least alleviate the disadvantages according to prior art mentioned above. For this purpose, an improved effectiveness as opposed to the indications mentioned above is to be achieved with a simple and safe application of the composition. Additionally, a composition having an improved effectiveness is to be provided with simultaneously reduced side effects.

In order to solve the problem mentioned above, the present invention – according to a first aspect of the present invention – provides a composition, in particular a pharmaceutical composition, according to claim 1. Further advantageous embodiments of the composition according to the invention are the object of the respective sub-claims.

A further object of the present invention – according to a further aspect of the present invention – is the packaging unit according to the invention according to claim 14, which contains the composition according to the invention, in particular in the form suitable for individual dosing, such as lozenges.

Finally, another object of the present invention – according to a further aspect of the present invention – is the use according to the invention of the composition according to the invention for the topical treatment of inflammatory diseases of the mouth and throat area, cough and catarrh of the upper respiratory system, according to claim 15.

It is understood that the designs, embodiments, advantages, and the like, which are stated below for only one aspect of the invention, for the purpose of avoiding repetition, of course, respectively also apply to the remaining aspects of the invention.

Furthermore, it is also understood that the relative or percentage, weight-based amounts stated, are to be selected by the person skilled in the art within the scope of the composition according to the invention such that the same will always supplement each other in the sum of 100% by weight, in consideration of the components, or active ingredients, or additives, or components, or excipients, respectively, in particular as defined below. This, however, goes without saying for the person skilled in the art. As to the rest, the person skilled in the art may deviate from the amounts stated below on an application or individual case basis, without departing the scope of the present invention.

The term "pharmaceutical preparation" – sometimes also characterized synonymous with "pharmaceutical composition," "pharmaceutical combination," etc. – is to be understood in a very broad sense of the present invention, and comprises any type of possible pharmaceutical preparation, composition, or combination, in particular pharmaceuticals, or drugs as such, but also so-called medical products, homeopathic agents, and the like.

The applicant has now surprisingly found that the problem described above may be solved in that, in particular, a pharmaceutical preparation, or composition, or combination, is formulated into a dosage form suitable for sucking, based on a combination of at least one first active ingredient component containing at least one tanning agent, or the extract thereof, with at least one second active ingredient component containing at least one mucilage drug, or the extract thereof. Such a composition is particularly suited for the production, in particular, of multi-phase lozenges, which lead to quick alleviation of the symptoms with inflammatory diseases of the mouth and throat area, as well as with cough and catarrh of the upper respiratory diseases, accompanied by accelerated healing of the diseases. In this context the applicant has most surprisingly found that the effectiveness of the composition according to the invention may be further increased, if the composition according to the invention is formulated into the form of a lozenge, having a particularly firm sheath, which contains the first active ingredient component having the tanning drug, and, in particular, a liquid core, which contains the second active ingredient component having the mucilage drug.

The object of the present invention – according to a first aspect of the present invention – is therefore a pharmaceutical composition in a dosage form suitable for sucking for the topical treatment of inflammatory diseases of the mouth and throat area, cough, and catarrhs of the upper respiratory system, wherein the composition comprises a combination of

(a) 0.05 to 30% by weight, based on the pharmaceutical composition, of at least one first active ingredient, containing at least one tanning agent in the form of an extract, having a drug/extract ratio in the range of 1:0.1 to 1:100, wherein the tanning agent is selected from *Pelargonium*, blackberry (*Rubus fruticosus*), oak (*Quercus rubor* and/or *Quercus petraea*), silverweed (*Potentilla anserina*), clove (*Syzygium aromaticum*), blueberry (*Vaccinium myrtillus*), myrrh (*Commiphora molmol*), Ratanhia (*Krameria triandra*), sage (*Salvia triloba*), blackthorn (*Prunus spinosa*), dead-nettle (*Lamium album*), common tomentil (*Potentilla erecta*), strawberry (*Fragaria vesca*), agrimony (*Agrimonia eupatoria*), lady's mantle (*Alchemilla xanthochlora*), rose (*Rosa gallica*), sanguisorba (*Sanguisorba officinalis*), and the combinations thereof; with

(b) 0.01 to 20% by weight, based on the pharmaceutical composition, of at least a second active ingredient, containing at least one mucilage drug in the form of an extract, having a drug/extract ratio in the range of 0.4:1 to 15:1, wherein the mucilage drug is selected from buckhorn plantain (*Plantago lanceolata* L.), Icelandic moss (*Lichen islandicus*), lady's finger (*Althaea officinalis* L.), hollyhock (*Malva sylvestris* L. and *M. neglecta* WALLR.), fenugreek (*Trigonella foenum-graecum* L.), salep and quince (*Cydonia oblonga* MILL.), and the combinations thereof;

in pharmaceutically effective amounts, wherein the composition has at least a first phase (A), and at least a second phase (B) being surrounded by the first phase (A), wherein the first phase (A) has at least the first active ingredient component (a), and the second phase (B) has at least the second active ingredient component (b), wherein the first phase (A) is embodied as a sheath, and the second phase (B) as a core, wherein the first phase (A) is present in a solid form, which is dissolvable during sucking, and/or under the influence of saliva, and wherein the second phase (B) is present in a liquid form, wherein phases (A) and (B) release the active ingredient components (a) and (b) during sucking and/or under the influence of saliva, in a time-delayed manner, wherein the first active ingredient component (a) is chronologically released before the second active ingredient component (b) during sucking and/or under the influence of saliva, wherein the composition contains the active ingredient components (a) and/or (b) independently of each other, each in a matrix, and/or a mass based on sugars and/or sugar substitutes, and wherein the ratio that is based on both the weight of the solid first phase (A) and the liquid second phase (B) is in the range of 50:98:50:2.

The combination mentioned above is particularly suitable for the prophylactic, and/or curative, in particular for the symptomatic prophylactic, and/or curative treatment of the diseases mentioned above. Furthermore, the combination mentioned above is particularly suitable for the temporary sole or auxiliary treatment of inflammation of the mouth and throat area, such as within the course of a cold, and the like. The use of nature-based active ingredients based on at least one tanning agent and at least one mucilage drug, results in a good tolerance, accompanied with the avoidance of side effects to the most possible extent, with a simultaneous high effectiveness of the composition according to the invention. The principle of effectiveness of the composition according to the invention is based on purely physical or physicochemical processes such that no receptor interaction is present in the pharmacological sense. The underlying principle of the present invention is based on a targeted combination of active ingredient component based both on tanning agents, and active ingredient components based on mucilage drugs, wherein the applicant has found very surprisingly that the effectiveness of the combination of both tanning agents and mucilage drugs may be further increased in reference of the diseases mentioned above, if the respective active ingredient components are administered in a time-delayed manner, as described in further detail below.

The extraordinary effectiveness of the combination according to the invention is based on a special adjustment of the mode of effect of both the tanning agent and the mucilage drug, wherein the individual effects supplement each other in a synergistic manner:

The mechanism of effectiveness of the tanning agents used within the scope of the present invention may – without intending to be bound to this theory – be understood such that the tanning agents initially cross-link the proteins in the mucous membrane of the mouth or throat with the administration of the composition according to the invention in the mouth and throat area, particularly upon the release thereof, such that a perfunctory aggregation, or formation of a protective membrane effectively results from cross-linked proteins. In this manner infections are prevented, or existing infections are alleviated. In this context the tanning agents used according to the invention also have an astringent effect, as well as antiviral and antibacterial properties such that the growth of bacteria, or the propagation of viruses, which have settled on the mucous membrane, for example, is effectively reduced, or prevented. In this manner, pain and wound secretion are reduced, inflammation is inhibited, and capillary hemorrhaging is stopped.

With regard to the mode of effect of the mucilage drugs used according to the invention, these may – without intending to be bound to this theory – be understood such that the mucilage drugs form a protective coating across the damaged mucous membrane with the release thereof within the scope of the administration of the composition according to the invention, wherein said formation of the coating leads to additional protection of the mucous membrane, accompanied by a quicker healing of the inflammation.

In this context the applicant has also surprisingly found that with the time-delayed release within the scope of the application of the composition according to the invention, according to which in chronological succession first the tanning agent and subsequently the mucilage drug are released, particularly good results are obtained with regard to the treatment of the diseases described above. Without intending to be bound to this theory, the surprisingly found improved effect based on a time-delayed release of both the tanning agent and the mucilage drug may be explained in that initially based on the tanning agents a cross-linking of the inflammatory proteins on the mucous membrane occurs, whereupon the mucilage drugs may form a protective mucilage coating over the same. For this purpose, the tanning agents, as mentioned above, initially cross-link the inflamed proteins of the (oral) mucous membrane; subsequently the mucous mucilage agents may adhere to the tanning agents, wherein the cross-linking of the mucilage agents is improved, in particular, because the not yet completely trapped tanning agents lead to the mucilage agent being better able to adherer to the inflamed tissue, thus being able to carry out the protective function thereof in a particularly advantageous manner.

With regard to the composition according to the invention, the same is embodied as a multi-phase system, in particular at least as a two-phase system, preferably as a two-phase system, wherein the respective phases are dissolved and/or released during sucking

and/or under the influence of saliva, wherein the respective phases release the active ingredients and/or the substances contained in the respective phases during sucking and/or under the influence of saliva in a time-delayed manner.

The term "phase," as used within the scope of the present invention, refers in particular to a differentiated embodiment of the composition according to the invention with regard to the dosage or application form thereof, such as in the form of lozenges. In this regard a phase may effectively represent a section or area of the dosage or application form of the composition according to the invention, which may differ with regard to the composition and/or the aggregate state thereof before use of a different phase – i.e., another area or section of the composition. For example, the composition according to the invention may, as will be further discussed below, have an exterior phase in a solid form, which may surround or envelope an additional internal phase in the manner of a sheath, such as in the form of a liquid core.

Within the scope of the present invention it is advantageous, if the active ingredient components (A) and (B) are contained in phases that differ from each other. In this manner, the time-delayed release of both the first active ingredient component (A) and the second active ingredient component (B) may be achieved with the application.

In other words, the composition according to the invention is embodied such that the composition or preparation according to the invention comprises multiple phases, in particular at least two phases, preferably two phases. For this purpose, it may be provided within the scope of the present invention that the respective phases each contain at least one active ingredient component, for example, a first phase may comprise at least the first active ingredient component (a), which contains at least the tanning agent, or the extract thereof. In this context, a second phase may contain the second active ingredient component (b) with at least one mucilage drug, or the extract thereof. In this regard it may be provided according to the invention – according to a preferred embodiment – that with the use of the composition according to the invention, in particular during sucking, the first active ingredient component (a) is initially chronologically released from the first phase, and subsequently, or chronologically subsequently the second active ingredient component (b) is released from the second phase. Generally, the term "time-delayed", as understood within the scope of the present invention, may also comprise a certain overlapping, or a certain transition of the release of the active ingredient or substance.

According to the invention it is provided that the composition according to the invention comprises at least a first phase (A) and at least a second phase (B), wherein the first phase (A) contains at least the first active ingredient component (a), and the second phase (B) contains at least the second active ingredient component (b). In this regard the phases (A) and (B) may release the active ingredient components (a) and (b) during sucking and/or under the influence of saliva, in a time-delayed manner. In this context the composition according to the invention should be such that the first active ingredient component (a) is contained at least essentially exclusively in phase (A), and the second active ingredient component (b) is contained at least essentially exclusively in phase (B).

According to a particularly preferred embodiment according to the invention the first phase (A) should surround the second phase (B), or essentially envelope the same. In this regard the first phase (A) is effectively embodied as a sheath ("jacket"), and the second phase (B) effectively as a core ("filling"). According to a particularly preferred embodiment according to the invention the result is therefore a core/sheath system, or a jacket/filling system, wherein the active ingredient component (b) is contained in the core, and the first active ingredient component (a) is contained in the sheath. During sucking, or under the influence of saliva, therefore, while the sheath, and therefore the phase (A) is being dissolved, a release of the first active ingredient component (a) and subsequently after dissolution of the sheath a release of the second active ingredient component (b) from the core, or from the phase (B) is the result. Therefore, initially the tanning agent, and subsequently the mucilage drug is released, which is a particular advantage in reference to the explanations given above with regard to effectiveness.

Within the scope of the present invention it is therefore provided according to a particularly preferred embodiment that the first active ingredient component (a) is chronologically released during sucking and/or under the influence of saliva before the second active ingredient component (b) is released.

With further regard to the composition according to the invention the composition may have a sheath, and at least one core being surrounded by the sheath. For this purpose, the sheath may contain the first active ingredient component (a), in particular the at least one tanning agent, and/or the extract thereof, and the core may contain the second active ingredient component (b), in particular the at least one mucilage drug, and/or the extract thereof. In this context the first phase (A) may be embodied as a sheath, and the second phase (B) may be embodied as a core.

According to the present invention it may further be provided that the composition according to the invention has at least two phases, in particular in the form of at least one exterior phase, and at least one interior phase, wherein the exterior phase comprises the active ingredient component (a), in particular the tanning agent, and/or the extract thereof, and the interior phase comprises the second active ingredient component (b), in particular the mucilage drug, and/or the extract thereof, in particular, wherein during sucking initially the active ingredient component (a) is chronologically released, and subsequently the active ingredient component (b) is released.

The applicant has also surprisingly found that even better results of the effectiveness of the composition according to the invention based on the targeted combination of both tanning agents with mucilage drugs, and the time-delayed release thereof, may be achieved, if – with regard to the ready-to-use composition according to the invention – the first active ingredient component (a) and/or the first phase (A), and/or the exterior phase and/or the sheath is/are present in a dissolvable form during sucking, and as a function of the first phase (A) the second active ingredient component (b), or the second phase (B), or the interior phase, or the core is/are present in liquid form.

The observations, or studies, respectively, of the application performed by the applicant show that with the targeted use of a liquid core containing the active ingredient component (b), and therefore the mucilage drug, the effectiveness of the composition according to the invention with regard to the named indications, is significantly improved. Without intending to be bound to any theory, this may be explained in that due to providing the core in liquid form during the release of the same, i.e. after dissolution of the solid sheath, or of the solid first phase (A) containing the active ingredient component (a), a better spatial distribution of the second active ingredient component (b), and therefore of the mucilage drugs results in the mouth and throat area, thus leading to an improved formation of the protecting coating formed by the mucilage drug on the (oral) mucous membrane. Furthermore, an administration of the composition according to the invention based on a specific combination of a solid sheath and a liquid core is perceived as pleasant, and the phase exchange occurring during sucking from the solid sheath to the liquid core also instills an indication in the user, at least on organoleptic level, of the dual or two-phase effect of the composition according to the invention. Also, a shorter application time results, as the liquid core does not require any dissolution during sucking, or contact with saliva.

Further it has been proven advantageous, if the second active ingredient component (b), and/or the second phase (B), and/or the core is embodied in a liquid, preferably viscous, in particular syrup-like, up to a paste-like, or even gel-like form. For this purpose the dynamic viscosity at room temperature (20°C), and ambient pressure (atmospheric pressure) of the second active ingredient component (b), and/or of the second phase (B), and/or of the core is in the range of 1 to 1,000 mPa·s, in particular 5 to 800 mPa·s, preferably 10 to 500 mPa·s, more preferred 15 to 300 mPa·s, particularly preferred 20 to 200 mPa·s. In this manner further optimizing results with regard to the release of the active ingredient component (b), since the matrix structure, in which the active ingredient component (b) is embedded, is further optimized, and the distribution is further improved due the special adjustment of the viscosity within the mouth.

With regard to the subsequent information as to the first active ingredient component (a) and the second active ingredient component (b) it should be mentioned that the first active ingredient component (a) contains the tanning agent(s), or is embodied from the same. The same applies to the second active ingredient component (b) accordingly, which equally contains the mucilage drug(s), or is embodied from the same.

With regard to the first active ingredient component (a), the first active ingredient component (a), i.e. the tanning agent, is added in the form of an extract, in particular a liquid extract, preferably in the form of a mother tincture; in this regard the extract is available based on an aqueous, alcoholic, or aqueous-alcoholic extract, preferably an aqueous-alcoholic extract.

Generally – and therefore also with regard to the second active ingredient component (b) – the use of an extract of a drug provides the essential advantage as opposed to the use of the drug as such, that high concentrations of the drug may be used such that a particularly good therapeutic effect is achieved. Additionally, any contaminations may be minimized in this manner.

In this context, particularly good therapeutic results are achieved, if the first active ingredient component (a), in particular the tanning agent, is added in the form of an extract, in particular a liquid extract, preferably in the form of a mother tincture, with a drug/extract ratio of 1:0.1 to 1:100, in particular 1:0.5 to 1:50, preferably 1:1 to 1:20, preferred 1:5 to 1:15.

With regard to the amount of the first active ingredient component (a), in particular of the tanning agent in the composition, or the combination according to the invention, said amount may vary widely. Generally, the composition according to the invention contains the first active ingredient component (a), in particular the tanning agent, and/or the extract thereof, in amounts of 0.05 to 30% by weight, in particular 0.1 to 20% by weight, preferably 0.2 to 10% by weight, preferred 0.5 to 5% by weight, based on the pharmaceutical composition. However, it may optionally be advantageous or necessary, depending on the application, to deviate from the amounts stated above.

According to the invention the tanning agent is selected from *Pelargonium*, in particular *Pelargonium sidoides*, and/or *Pelargonium reniforme*, blackberry (*Rubus fruticosus*), oak (*Quercus rubra* and/or *Quercus petraea*), silverweed (*Potentilla anserina*), clove (*Syzygium aromaticum*), blueberry (*Vaccinium myrtillus*), myrrh (*Commiphora molmo*), Ratanhia (*Krameria triandra*), sage (*Salvia triloba*), blackthorn (*Prunus spinosa*), dead-nettle (*Lamium album*), common tormentil (*Potentilla erecta*), strawberry (*Fragaria vesca*), agrimony (*Agrimonia eupatoria*), lady's mantle (*Alchemilla xanthochlora*), rose (*Rosa gallica*), sanguisorba (*Sanguisorba officinalis*), and the combinations thereof, in particular *Pelargonium sidoides*, and/or *Pelargonium reniforme*.

Within the scope of the present invention it is particularly advantageous, if the first active ingredient component (a), in particular the tanning drug, is *Pelargonium*, in particular *Pelargonium sidoides*, and/or *Pelargonium reniforme*, or comprises the same, in particular in the form of an extract, preferably a liquid extract, preferably in the form of a mother tincture. For example, the component of *Pelargonium* extract is an aqueous-ethanol extract from the root of *Pelargonium sidoides*, or *Pelargonium reniforme*. Within the scope of the present invention, a mother tincture from *Pelargonium sidoides* may be utilized, for example, in which the drug utilized is *Pelargonium sidoides* radix. Said mother tincture may have a drug/mother tincture ratio of about 1:8-9, and a drug/extract ratio of about 1:10. For example, ethanol 15% (m/m) may serve as the extract in this regard, for example, produced from ethanol 96% Ph. Eur. and purified water Ph. Eur. This mother tincture is a clear, brown liquid. The dry residue of this mother tincture may be about 1% according to Ph. Eur.

The species mentioned above comprise tanning agents, which interact with the inflamed proteins of the (mouth) and throat mucous membrane within the scope of the present invention, as described above, and which, in addition to having an astringent effect, are also pain-relieving, hemostatic, secretion-inhibiting, mucous membrane-protecting, antimicrobial, bactericidal, fungicidal, and anti-inflammatory. The astringent effect is based in particular on an interaction with protein molecules of collagen fibers of the uppermost

tissue layers of the mucous membrane. In particular, tanning agents having a molecular weight of between 500 and 3,000, and having 1 to 2 hydroxyl groups per 100 mass units, show this effect. Due to their chemical properties, the agent classes of the tanning agents are subdivided into condensed and hydrolysable tanning agents. Examples of condensed tanning agents are, e.g. catechine tanning agents and proanthocyanidines.

The modules of the condensed catechine tanning agents are the flavanols (+)-catechin and (+)-epicatechin. Mixed condensates also occur, which additionally contain leuco-anthocyanidines, and are defined as proanthocyanidines. The hydrolysable tanning agents may be cleaved into sugar and gallic acid, or ellagic acid (hexahydroxy diphenic acid) by means of hydrolysis. Therefore, a differentiation is made between gallotannins and ellagitannins. A typical representative is "tannin" (hexagalloyl glucose), or digallic acid. Often, mixed compounds also occur, which also result in gallic acid as well as catechin with hydrolysis, such as epicatechin gallate.

With regard to the *Pelargonium* species preferably used according to the invention, in particular *Pelargonium sidoides*, and/or *Pelargonium reniforme*, the total tanning agent content in these species in the roots is about 9% of the dry mass. For this purpose, the content of hydrolysable tanning agents is very low, as the counts found for gallic acids are less than 0.01% in the dry mass, and are approximately 0.02% in the dry mass for gallic acid methyl ester. Therefore, the catechin tanning agents are dominating, for which mostly catechin and gallocatechin, and in small amounts also afzelechin have been detected as monomers. These monomers are present in a complexly composed mixture of polymer structures of at least eight flavanol units, the molecular weight of which is approximately 2,300, and is therefore still within the range of an astringent effect.

With regard to the mechanism of effect in terms of the adsorption of tanning agents on proteins, this may also be understood such that – without intending to be bound to this theory – upon the contact of tanning agents with protein molecule, an adsorption of the substance to the open, or amorphous, non-quasi crystalline sections of the protein molecules occurs initially. For small concentrations of astringents, or tanning agent, respectively, as compared to the amount of protein, a linear dependency of the adsorption of the concentration is measured. These circumstances of a linear relationship between the tanning agent adsorption and the concentration is utilized in the analytics of tanning agents. Experimentally, the tanning agent is completely bound due to a high excess of skin powder (proteins), and the same is illustrated by the difference of the optical extinction of a dye reaction before and after adsorption. With another addition of tanning agent, the adsorption count will near a threshold value. The curve resulting from this (adsorption versus concentration) is completely different from a pharmacological dose/effect relationship. The present conditions are known from physical chemistry, and are usually described by the Langmuir Equation for adsorption isotherms. The Langmuir Law of adsorption may be represented as a function of the adsorbed amount depending on the concentration. The saturation value described herewith results from the formation of so-called "monolayers," and therefore a saturation of the available surface of the protein molecules with the tanning agent. Therefore, the formation of "monolayers" by means of tanning agents on protein molecules and the cross-linking of proteins by means of said tanning agent layer is described.

An astringent effect occurs, if the tanning agent cross-links the protein molecules (e.g. in collagen fibers) by means of less stable ion or hydrogen bridge compounds. These actions are the basis of the effect of the composition according to the invention on the mucous membrane in the mouth, as relatively little tanning agent, and a large amount of protein are present. Due to the relatively low amount of tanning agents present, the same are bound to the mucous membrane of the mouth, but may not penetrate the epithelium barrier, and are therefore not resorbed.

In summary it may be therefore determined that the released tanning agents of the composition according to the invention, being in particular comprised of *Pelargonium* extract, cross-link the proteins of the inflamed mucous membrane in the mouth and throat due to their astringent properties, wherein the same are physicochemical or physical mechanisms of effect of the adsorption and ion

compounds, which are not considered as belonging to the pharmacological effects by definition. Due to the mechanism of effect of the surface adsorption, the tanning agents are at least essentially also not resorbed in the mouth area.

With regard to the preferably utilized *Pelargonium* species, this plant, also called Kap-Pelargonium, originally comes from South Africa. In addition to *Pelargonium sidoides*, many very similarly looking *Pelargonium* species are utilized as traditional medicinal plants, and also as nutrition, as well as for other purposes (e.g. perfume) in South Africa. Due to the known non-toxicity, the leaves and stems of all types are gladly consumed as "bush food snack," but also the roots are harvested as vegetables for food supply.

With regard to the mucilage drug contained in the second active ingredient component (b), the same is added in the form of an extract, in particular of a dry extract. In this regard the extract is available based on an aqueous-alcoholic, or aqueous-alcoholic extract, preferably an aqueous extract. Insofar as the active ingredient component (b), in particular the mucilage drug, is utilized in the form of a dry extract, the same should preferably be at least essentially water-soluble.

The drug/extract ratio may vary widely. If the second active ingredient component (b), in particular the mucilage drug, is utilized in the form of an extract, preferably a dry extract, the drug/extract ratio should be selected, in particular, in the range of 0.4:1 to 15:1, in particular in the range of 1:1 to 10:1, preferably in the range of 5:1 to 8:1.

With regard to the amount of the second active ingredient component (b), in particular of the mucilage drug, or the extract thereof, said amount may vary widely. Generally, the composition according to the invention comprises the second active ingredient component (b), in particular the mucilage drug, and/or the extract thereof, in amounts of 0.01 to 20% by weight, in particular 0.05 to 10% by weight, preferably 0.05 to 5% by weight, preferred 0.08 to 2% by weight, based on the pharmaceutical composition.

Mucilage drugs utilized according to the invention, which are contained in the second active ingredient component (b), are selected from buckhorn plantain (*Plantago lanceolata* L.), Icelandic moss (*Lichen islandicus*), lady's finger (*Althaea officinalis* L.), hollyhock (*Malva sylvestris* L. and *M. neglecta* WALLR.), fenugreek (*Trigonella foenum-graecum* L.), salep and quince (*Cydonia oblonga* MILL.), and the combinations thereof, preferably buckhorn plantain (*Plantago lanceolata* L.).

A preferred embodiment according to the invention, according to which the second active ingredient component (b), in particular the mucilage drug, is buckhorn plantain (*Plantago lanceolata* L.), or comprises the same, in particular in the form of an extract, in particular a dry extract, in particular, wherein the extract is obtained based on an aqueous, alcoholic, or aqueous-alcoholic extract, preferably an aqueous extract. This mucilage drug supplies the best results within the scope of the present invention.

Mucilages are heteropolysaccharides having molecular weights of approximately 50,000 to 2,000,000, which are gained from the drug by means of extraction in hot or cold water. Contrary to the rubbers, the highly viscous solutions are not sticky. A differentiation can be made between acidic and neutral mucilages. Depending on their sugar composition, they may be subdivided into glucomannans or mannans, into galactomannans, xylans, or rhamnogalacturonans. After localization of the same in the plant, a differentiation may be made between vacuole mucilages and membrane mucilages. The mucilage of the lady's finger roots may be seen as a prototype for an acidic plant mucilage. It contains L-rhamnose, D-galactose, D-galacturonic acid, and D-glucuronic acid in a molar ratio of about 3:2:3:3. The most simply constructed part of the polysaccharide consists of repeating undecasaccharide sub-units.

Buckhorn plantain (*Plantago lanceolata* L.) grows in all of Europe, as well as in Northern and Central Asia. The drug comes from wild growing plants and cultures, mainly from Southeast Europe. The dried, olive to brownish-green colored, lanceolate leaf blades, having about three to seven parallel extending nerves, may be used. The herbal drug consists of the dried leaves, stems and whole blossoms. In addition to the mucilage, buckhorn plantain also contains tannin as an additional substance, iridoid glycoside aucubin (1.9 to 2.4%), which is responsible for the dark coloring of a not carefully dried drug, and is utilized for identity testing, and

furthermore the mustard oil sulfuraphen. Buckhorn plantain, in particular the leaves of the buckhorn plantain, is particularly utilized in the form of teas and syrups for inflammation of the mouth and throat area.

Icelandic moss is the colloquial name for *Lichen islandicus*, or *Cetraria islandica* (Parmeliaceae), a lichen – contrary to the colloquial name it is not a moss –, which is exported from Northern countries, such as Iceland, Norway, and Sweden. Icelandic moss, in the classical meaning, consists of the dried thallus of *Cetraria islandica*, as well as the preparations thereof. The drug contains, among others, mucilage drugs and bitters, as well as bitter-tasting lichenic acids. From the powdered lichen, about 60% by weight are dissolved during boiling with a strongly diluted sodium hydrogen carbonate solution, and a gelatin is created during the cooling off of the solution. The extract consists of a polysaccharide mixture of lichenin and isolichenin, a number of bitter-tasting lichenic acids (fumar protocetraric, protocetraric, and cetraric acid), as well as protolichestic acid, which converts into lichestic acid and usnic acid during processing as a lichen dye having an antibiotic effect. As a mucilage drug, Icelandic moss possesses irritation-alleviating properties, and it also acts as an antimicrobial. The bitter content justifies its use for loss of appetite. Icelandic moss is applied, for example, with catarrhs and diarrhea, as a bitter tonic, topically on slow healing wounds, in cosmetic preparations, in hair setting lotions, as an additive in sponge cake flour, and the like, for loss of appetite, as well as irritations of the mucous membrane in the mouth and throat area. A mouth and throat deficiency, based on Icelandic moss, has an irritation-alleviating effect on dry cough. The cold macerate, and other bitter-tasting preparations of the drug, are utilized for eliminating the subacidity or antacidity. As a dosage form the crushed drug is utilized, depending on the field of application, for infusions, as well as for other galenic preparations, or the crushed drug is preferably utilized for cold macerates, as well as other bitter-tasting preparations for ingestion. For further details on Icelandic moss, reference may be made, for example, to the following cited literatures: Römpf Chemical Dictionary, 9th Edition, Volume 3, Georg Thieme Verlag, Stuttgart/New York, 1990, pages 2055/2056, keyword: "Icelandic moss"; HagerROM 2001, Springer Verlag, Heidelberg, keywords: "Cetraria," "Cetraria ericetorum OPZ," "Cetraria islandica (L.) ACHARIUS," and "Lichen islandicus (Icelandic moss)," Monographie "Lichen islandicus (Icelandic moss)," Bundesanzeiger No. 43 of March 2, 1989; H. Wagner, "Pharmaceutical Biology – Drogen und ihre Inhaltsstoffe," Gustav Fischer Verlag, Stuttgart/New York, 1984, page 281, keyword: "Cetrariee Lichen (= Lichen islandicus – Icelandic moss)."

Lady's finger (*Althaea officinalis* L.), utilized in the form of the lady's finger root, leaves, and blossoms, grows on saliferous and moist ground in Central, Eastern and Southeastern Europe. The root branches and side roots freed from the ligneous main root, root fibers and bark layers, harvested in fall, and dried at 35°C, are sold on the market in peeled and unpeeled varieties. The brown coloring of the peeled drug is a quality defect; any retrospective "beautification" using a sulfite solution is not permitted. Furthermore, the grey felt-pubescent dried leaves, collected before or after blooming, being about 10 cm long, about 8 cm wide, having three to five lobes, as well as the dried, flesh-colored petals, collected in July/August, are utilized. Lady's finger is a herbaceous perennial of about 1 m height, which is propagated either generatively or vegetatively. The root harvested in late fall contains up to 15% of mucilage drug. In spring and summer the mucilage content is 5 to 6%. The mucilage content of the leaf and blossom drug is 6 to 9%. The mucilage is localized in the root in certain mucilage cells of the bark and wood parenchymas. It consists of galacturonorhammans, glucans, and arabinogalactans. Aqueous extracts from the root are to be determined by means of maceration at room temperature, so that the abundant starch will not interfere with swelling. Lady's finger drugs are used for tea preparations, or for the production of *Sirupus Althaeae*. The main field of application is inflammatory irritation conditions of the throat area. Externally, lady's finger is used for softening compresses, baths, and cataplasms.

Hollyhock (*Malva sylvestris* L. and *M. neglecta* WALLR.), in particular used in the form of hollyhock blossoms and leaves, is native to Europe, Asia Minor, in the Mediterranean Region, and on the Indian subcontinent. For this purpose, the pink-violet colored blossoms, which are collected during blossoming, or the strongly shriveled, folded leaves, which are mostly sold in the form of packages, are

used. Hollyhock is a perennial herb that grows two to multiple years. The mucilage content of blossoms and leaves is 6 to 8%. With hydrolysis, the mucilage supplies glucose, arabinose, rhamnose, and galactose. Hollyhock blossoms are used in gargling solutions and baths, and are used together with the leaves in tea mixtures as expectorants.

Fenugreek (*Trigonella foenum-graecum* L.), in particular used in the form of fenugreek seed, is native to the entire Mediterranean region, as well as Eastern Europe, India, and China. The main drug import comes from the cultures of India and Morocco. For this purpose, the brownish-red colored, four-sided and diamond-shaped, flat, very hard seeds that are about 5 mm long and about 3 mm wide, which are characterized by a notch, are used. In addition to fatty oil, the drug also contains 20 to 30% mucilage, trigonellin, nicotinic acid amide, choline, bitter, and saponins. The production of the mucilage is carried out using powdered seeds. The powder is used topically for compresses for furuncles, tumors, and swollen glands, internally as expectorants and roborants.

Salep, or Salep Tuber, in particular used in the form of the salep bulb, is derived from various orchid species, in particular from *Orchis mascula* L., *Orchis morio* L., *Orchis militaris* L., *Anacamptis pyramidalis* L. RICH. and *Platanthera bifolia* L. RICH. For this purpose, the about 4 cm long to about 3 cm thick, wrinkled, hard, brownish bulbs, which are freed from their basket layer, blanched with boiling water, and dried at artificial heat, are used. Salep mucilage, which mainly consists of up to 50% glucomannan, or glucan, is mainly used in pediatric natural healing as an antidiarrheal.

Quince (*Cydonia oblonga* MILL.) is native to Southeastern Arabia. The main drug imports come from Spain, Portugal, and Persia. The ripe, dried, reddish-brown to brownish-violet colored, slightly flattened seeds of the quince spurious fruit are used. The seeds are partially equipped with a dried mucilage crust on the exterior, and are often adhered to one another. They have a weak bitter almond taste. Inside of the epidermis is approximately 22% mucilage, which is largely water-soluble. The sugar components are arabinose, xylose, and uronic acid, which is partially methylated. The drug is utilized only in its uncrushed state. The quince mucilage is used topically for lip and nipple fissures, for burns and bedsores in the form of ointments and creams.

Particularly good results according to the invention are achieved with buckhorn plantain (*Plantago lanceolata* L.).

For further details on mucilage drugs and the preparations, effects, and applications thereof, reference may be made to H. Wagner "Pharmazeutische Biologie – Drogen und ihre Inhaltsstoffe," Gustav Fischer Verlag, Stuttgart/New York, 1985, in particular pages 280 and following.

As mentioned above, the mucilage drug should be added in the form of an extract, in particular of a dry extract. Such dry extract is advantageously available based on an aqueous, alcoholic, or aqueous-alcoholic extract, preferably based on an aqueous extract (e.g. by means of commonly used methods, such as stripping the water and/or alcohol under vacuum, optionally while heating, lyophilization, etc.). Advantageously, a dry extract of *Plantago lanceolata* may be utilized within the scope of the invention, wherein *Plantago lanceolata* folia is utilized as the drug parts. Ethanol (e.g. 40% by volume) may be used as the extracting agent. For this purpose, the drug/extract preparation ratio may be, for example, about 4:1, and the drug/drug preparation (native extract) may be, for example, about 4.2-5.5:1. The native extract proportion may be in the range, for example, of about 72 to 95% by weight, based on the extract preparation. This dry extract is a brownish-green fine powder, having a weak odor, and a slightly bitter taste.

The composition according to the invention should contain the active ingredient components (a) and/or (b), in particular the tanning agent, and/or the mucilage drug, each in a matrix and/or mass, in particular, wherein the first active ingredient component (a), in particular the tanning agent, is embedded in a solid matrix and/or mass, which is soluble, in particular, during sucking and/or under the influence of saliva, and/or in particular, wherein the second active ingredient component (b), in particular the mucilage drug, is embedded in a liquid matrix and/or mass, which is soluble in particular during sucking and/or under the influence of saliva.

in this context the composition according to the invention should contain the active ingredient components (a) and/or (b), in particular the tanning agent and/or the mucilage drug, independently of each other, each in a matrix and/or mass, based on sugars and/or sugar substitutes.

With further regard to the composition according to the invention, the same may contain sugar and/or sugar substitutes in amounts from 50 to 99.6% by weight, in particular 60 to 99.5% by weight, preferably 70 to 99% by weight, particularly preferred 80 to 98.8% by weight, most particularly preferred 90 to 98.5% by weight, based on the pharmaceutical composition.

For this purpose, the sugars should be selected from the group of saccharose, glucose, in particular dextrose, and fructose. The sugar substitutes should be selected from sugar alcohols, and/or from the group of mannitol, lactate, leucrose, fructooligosaccharides, glucans, and polyglucose.

It is particularly advantageous, if the first phase (A) containing the first active ingredient component (a), and/or the sheath, contains isomalt, in particular liquid isomalt, in particular in amounts of 70 to 95% by weight, in particular 75 to 90% by weight, preferably 80 to 90% by weight, based on phase (A), and/or the sheath. Furthermore, the first phase (A) containing the first active ingredient component (a), and/or the sheath, may contain maltite, in particular maltite syrup, in particular in amounts of 2 to 20% by weight, in particular 3 to 18% by weight, preferably 5 to 15% by weight, based on phase (A), and/or the core.

Furthermore, the invention may provide that the second phase (B) containing the second active ingredient component (b), and/or the core, contains maltite, in particular maltite syrup, in particular in amounts of 50 to 95% by weight, in particular 60 to 90% by weight, preferably 70 to 85% by weight, based on the second phase (B), and/or the core.

In an embodiment preferred according to the invention, the composition according to the invention is present in a dosage form based on lozenges, in particular in the form of hard candy, a pastille, or tablet. The dosage form may be formed on the basis of lozenges, in particular in the form of multi-phase, preferably two-phase lozenges, preferably having at least one, preferably solid, core, and/or a solid first phase (A), containing the first active ingredient component (a), and having a liquid core, and/or a liquid second phase (B), containing the second active ingredient component (b).

In this context the dosage form of the composition according to the invention should release a therapeutically effective amount each of the first active ingredient component (a), in particular the tanning agent, and of the second active ingredient component (b), in particular the mucilage drug, during sucking and/or under the influence of saliva, in a time-delayed manner, once the dosage form has been administered and is sucked in the mouth area of the patient, wherein initially the first active ingredient component (a), in particular the tanning agent, and subsequently the second active ingredient component (b) are released chronologically.

In this context it has been proven advantageous, as stated above, if the composition is present, in particular, in the form of a lozenge having a solid sheath, and/or a solid first phase (A), and having a liquid core, and/or a liquid second phase (B).

In other words, the basic principle of the present invention is therefore that the *Pelargonium* component, and subsequently, or chronologically offset, the buckhorn plantain component are released, i.e. the *Pelargonium* and buckhorn plantain components are chronologically released in succession, wherein the present invention also comprises such embodiments, in which a certain overlapping of each respective release of both the *Pelargonium* components and the buckhorn plantain components is present. As mentioned above, a particularly good effectiveness results from the offset release. In this context the solid embodiment of the sheath, or of the first phase (A), with the active ingredient component (a) ensures that low amounts of the tanning agents are released over a chronologically relatively long time, which is advantageous with regard to the interaction with the (oral) mucous membrane. By releasing the second active ingredient component (b) from the liquid phase (B), or from the liquid core, a quick and effective formation of the mucilage layer on the (oral) mucous membrane previously treated with the tanning agent, is achieved, leading to a further improved effectiveness of the composition according to the invention.

As described above, the pharmaceutical preparation according to the invention is particularly suited for the prophylactic and/or therapeutic treatment of inflammatory diseases of the mouth and throat area, irritations of the mucous membrane, and mucous membrane lesions in the mouth and throat area, drying of the mucous membrane in the region of the mouth and throat area, cough, and tussive irritation, in particular dry cough, hoarseness, bronchial catarrhs, and bronchial asthma. In this context, the pharmaceutical preparation according to the invention is applied topically, or perorally.

The production of the pharmaceutical preparation according to the invention may be carried out in the manner already known. For further details, reference may be made to the following exemplary embodiments.

In this context, the composition according to the invention should be present, in particular, in the form of lozenges, having a total weight of 1 to 6 g, preferably 1.5 to 5 g, particularly preferred 2 to 4 g.

For this purpose, the weight-based ratio of the solid sheath, and/or of the solid first phase (A) to the liquid core, and/or the liquid second phase (B) should be in the range of 50:98:50:2, in particular 60:95:40:5, preferably 70:90:30:10.

Furthermore, the dosage form, in particular the lozenge, should contain 10 to 500 mg, in particular 20 to 400 mg, preferably 30 to 300 mg of the first active ingredient component (a), in particular of the tanning agent, and/or the extract thereof, in particular, wherein the first active ingredient component (a), in particular the tanning agent, and/or the extract thereof, is at least essentially exclusively contained in the solid sheath, and/or in the solid first phase (A). Preferably, the first active ingredient component (a), in particular the tanning agent, or the extract thereof, should therefore be at least essentially exclusively contained in the solid sheath, and/or the solid first phase (A).

Furthermore, the dosage form, in particular the lozenge, should contain 5 to 250 mg, in particular 10 to 200 mg, preferably 15 to 150 mg of the second active ingredient component (b), in particular of the mucilage drug, and/or the extract thereof. In this context, the second active ingredient component (b), in particular the mucilage drug, or the extract thereof, should be contained at least essentially exclusively in the liquid core, and/or in the liquid second phase (B).

The dosage form, in particular the lozenges, may further 1.5 to 4.9 g, in particular 1.5 to 2.9 g of sugar, and/or sugar substitutes.

The information on the weight mentioned above with regard to the first active ingredient component (a), which contains or represents the tanning agent, of the second active ingredient component (b), which contains or represents the mucilage drug, as well as the sugars, or the sugar substitutes, are based on the dosing unit, in particular in the form of a lozenge.

Furthermore, the invention may provide that the composition according to the invention contains additional active ingredients and/or substances, in particular selected from the group of processing aids, aromatics, flavorings, sugar substitutes, sweeteners, acidifiers, stabilizers, and/or antiseptics.

These are known to the person skilled in the art, and the person skilled in the art is readily able to select the respective additional active ingredients or substances in terms of their type and amount within the scope of the composition according to the invention, and to adjust each to one another.

The composition according to the invention may be used by means of sucking, e.g. in the case of colds, by means of which the cold symptoms are significantly alleviated, and additionally tussive irritation caused by a reflex may be reduced. Due to the mechanical stimulation of sucking, the formation of saliva is additionally prompted, which is equally of advantage. The tanning agents, coming in particular from *Pelargonium* types, such as *Pelargonium sidoides* and/or *Pelargonium reniforme*, cross-link the mucous membrane proteins with the use, and accelerate healing of the already affected mucous membrane. The irritation alleviating mucilage drugs, in particular from *Plantago lanceolata*, form a film on the inflamed mucous membrane, and protect it from further attacks by means of dry and optionally contaminated inhaled air, and reduce the tussive irritation caused by a reflex. Therefore, within the scope of the present invention, a triple physical protection from increased salivation, as well as from the tanning agent and mucilage drugs results.

leading to a significant alleviation and quicker healing. Due to the preferred embodiment according to the invention having the time-delayed release of both the tanning agent and the mucilage drug, the effectiveness is further increased. As explained above, the extraordinary effectiveness of the composition according to the invention may be further increased, if the tanning agent is incorporated in a solid sheath, and the mucilage drug is incorporated in a liquid core.

A further object of the present invention – according to a further aspect of the present invention – is a packaging unit according to the invention, in particular a blister package, containing the composition defined above, in particular in the form of a form suitable for single doses, preferably in the form of lozenges. The packaging unit according to the invention preferably contains a plurality of lozenges, in particular for individual removal.

Another object of the present invention – according to yet a further aspect of the present invention – is the use according to the invention of the composition according to the invention, as defined above, for the topical treatment of inflammatory diseases of the mouth and throat area, cough, and catarrhs of the upper respiratory system, or the use according to the invention of the composition according to the invention, as defined above, for the production of a pharmaceutical for the topical treatment of inflammatory diseases of the mouth and throat area, cough, and catarrhs of the upper respiratory system.

In this context the composition according to the invention should be prepared for administration of 10 to 5,000 mg, in particular 60 to 3,000 mg of the first active ingredient component (a), in particular of the tanning agent, and/or the extract thereof, and 5 to 2,500 mg, in particular 30 to 1,200 mg of the second active ingredient component (b), in particular of the mucilage drug, and/or the extract thereof, per day with an administration of 1 to 12 dosage units, in particular in the form of individual lozenges. Preferably, 3 to 6 dosage units should be administered per day, wherein the administration should occur every 2 to 3 hours.

Further embodiments, deviations, and variations, as well as advantages of the present invention are readily recognizable and realizable for the person skilled in the art reading the description without departing from the scope of the present invention.

The following exemplary embodiments serve merely for illustration of the present invention, however, without being limited thereto.

Exemplary Embodiments:

Production Example:

A pharmaceutical preparation according to the present invention in the form of a lozenge, having a solid sheath and a liquid core, is produced based on the following compositions for the solid sheath and the liquid core. The following percentages are based on the total preparation with the sheath and core composition.

1. Composition for the solid sheath:

Matrix components based on sugars	
and sugar alcohols	79.4442% by weight
Pelargonium mother tincture (1:8-9)	3.3354% by weight
Processing aids, aromatics,	
flavorings, acidifiers	<u>0.5204% by weight</u>
Total approximately	83.3000% by weight
Residual moisture (2%)	<u>1.7000% by weight</u>
Sheath	85.000% by weight

2. Composition for the liquid core:

Matrix components based on sugars

and sugar alcohols	11.8731% by weight
Buckhorn plantain powder extract (4:1)	0.8343% by weight
Processing aids, aromatics, flavorings, acidifiers	<u>0.0425% by weight</u>
Total approximately	12.7499% by weight
Residual moisture (15%)	<u>2.2500% by weight</u>
Sheath	15.000% by weight

The respective compositions for the sheath and for the core are processed into lozenges according to the invention, having a solid jacket, or having a solid sheath, and having a liquid core, or having a liquid filling, wherein with regard to the production of the sheath, a base mixture is initially produced from the matrix components, and after pre-dissolving and boiling, a vacuum process follows. Subsequently, the additional components are added, including the *Pelargonium* mother tincture. The mass is pumped onto a cooling conveyor, and tempered. A tapered roller is equipped with the mass that is produced in this manner. With regard to the filling, or the liquid core, a filling is initially cooked from the materials used for this purpose, and the required residual moisture content is adjusted. The filling, or the core, is continuously fed into the sugar cone of the tapered roller by means of a filling pipe; subsequently the lozenges according to the invention are molded on a special drawing and embossing machine at the predetermined dimension. The weight of the lozenge according to the invention is adjusted to about 3 g. The sheath/core ratio is about 85:15. The lozenges according to the invention are placed in bulk cartons via a cooling system and a subsequent sorting and control line. Subsequently, respective blister packages may be filled.

Application observations or effectiveness studies:

1.) 15 patients at the age of 28 to 45 years, having an irritation of the mucous membrane in the mouth and throat area due to colds, were treated with the pharmaceutical preparation described in the above production example, based on lozenges having a solid sheath and a liquid core, wherein six tablets each were administered per day for a period of ten days (group A).

Additional 15 patients at the age of 31 to 42 years, having symptoms comparable to those in group (A), were treated with lozenges having a tincture content comparable to the production example. The lozenges had a solid sheath and a solid core. The composition was applied at six lozenges each day for a period of ten days (group B).

Another patient group, comprising ten patients at the age of 31 to 45 years, having the symptoms described above, were administered a mono-preparation, based on a solid lozenge, which merely contained a tanning agent based on *Pelargonium*. The content of *Pelargonium* mother tincture corresponded to the content described in the production example (group C).

Within the scope of another test group comprised of ten patients at the age of 31 to 48 years, lozenges of the type of a mono-preparation were administered, wherein the tables were present in solid form, and contained only a *Plantago* mucilage drug. The content of the *Plantago* powder extract corresponded to the content described in the production example. Over a time period of ten days, six lozenges were administered per patient and per day (group D).

While in all patients of group A the symptoms had already stopped completely after five days, i.e. the inflammatory symptoms on the mucous membrane of the mouth and throat could no longer be observed, it was observed that the symptoms of eight patients in group B abated after six days, while two patients of group B saw their symptoms abate after seven days. Both the subjects of group A and the subjects of group B reported already on day one of the administration of the respective composition a significant alleviation of

the symptoms. Furthermore, all subjects of group A evaluated the sucking sensation of the lozenge according to the invention as very pleasant, in particular, the "dissolution" of the liquid core was perceived as beneficial.

With the subjects of group C, a significant alleviation or healing of the symptoms could be observed in eight subjects after nine days, while in two of the subjects a complete abatement of the symptoms still had not occurred, even after ten days. With regard to the subjects of group D, three patients still had distinct symptoms in terms of inflammatory mucous membrane irritation, in five patients only weak symptoms were observed, while two patients were nearly free of all symptoms after ten days.

The studies show that the use of the preparation according to the invention in the form of a combination of tanning agents and mucilage drugs, with a time-delayed release of each respective component and the liquid core, effects a significantly increased therapeutic success, as an improved therapy success – elimination of the symptoms – is achieved with the preparation according to the invention. Furthermore, the use of the composition according to the invention was also perceived as pleasant by the subjects.

In the treatment of irritations of the mucous membrane of the mouth and throat area, the pharmaceutical preparation according to the invention leads to an impressive improvement of the accompanying symptoms. This represents a crucial advantage of the combination according to the invention.

2.) Within the scope of the study the antiviral effect of the composition according to the invention, as it is described in the production example, was compared to that of the mono-preparation, as it was utilized with regard to group D. In this regard saliva samples were taken daily from the subjects of group A and groups C and D, and the virus titer of viruses typically present in a cold, was determined in this regard. In the subjects of group A reduced virus titers were determined as compared to the subjects of groups C and D, which substantiates the effectiveness of the composition according to the invention.

TOROK CUKORKA KOMPOZÍCIÓ A SZÁJ ÉS A GARAT GYULLADÁSOS BETEGSÉGEINEK KEZELÉSÉRE SZABADALMI IGÉNYPONTOK

1. Gyógyászati kompozíció torok cukorkakénti (négyzetes cukorka) (lozengé) adagolási formában a száj és a torok terület gyulladós betegségeinek, köhögésnek és a felső légúti rendszer hurutjának helyi kezelésére, ahol a kompozíció a következőknek kombinációját tartalmazza:

a gyógyászati kompozícióra alapozva 0,05 és 30 tömeg % közötti tartományban legalább egy első aktív alkotórész, amely legalább egy cserző szer (tanning agent) tartalmaz kivonat (extraktum) formájában, amelynek gyógyszer/kivonat aránya az 1:0,1 és az 1:100 közötti tartományban van, ahol a cserző anyag a következők közül választható ki: gólyaorr (*Geranium*), földi szeder (blackberry) (*Rubus fruticosus*), tölgy (oak) (kocsányos tölgy és kocsánytalan tölgy) (*Quercus rubor* és/vagy *Quercus petraea*), lipapimpó (silverweed) (*Potentilla anserina*), szegfűszeg (clove) (*Syzygium aromaticum*), fekete áfonya (blueberry) (*Vaccinium myrtillus*), illatos mirhafű (myrrh) (*Commiphora molmoli*), Ratanhia (*Krameria triandra*), zsálya (sage) (*Salvia triloba*), kökény (blackthorn) (*Prunus spinosa*), árvacsalán (dead-nettle) (*Lamium album*), vérontó pimpó (common tormentil) (*Potentilla erecta*), földieper (strawberry) (*Fragaria vesca*), apróbojtorján (agrimony) (*Agrimonia eupatoria*), közönséges palástfű (lady's mantle) (*Alchemilla xanthochlora*), rózsa (rose) (*Rosa gallica*), csabaire vérfű (sanguisorba) (*Sanguisorba officinalis*), és mindezek kombinációi; a következők:

a gyógyászati kompozícióra alapozva 0,01 és 20 tömeg % közötti tartományban legalább egy második aktív alkotórész, amely legalább egy nyálkaképző gyógyszert (mucilage drug) tartalmaz kivonat (extraktum) formájában, amelynek gyógyszer/kivonat aránya a 0,4:1 és a 15:1 közötti tartományban van, ahol a nyálkaképző gyógyszer a következők közül választható ki: lándzsás útifű (buckhorn plantain) (*Plantago lanceolata* L.), izlandi zuzmó (Icelandic moss) (*Lichen islandicus*), orvosi ziliz (lady's finger) (*Althaea officinalis* L.), mályva (hollyhock) (erdei mályva és papsajtmályva) (*Malva sylvestris* L. és *Malva neglecta* WALLR.), görögcséna (fenugreek) (*Trigonella foenum-graecum* L.), kosborgyökér (salep) és birs (quince) (*Cydonia oblonga* MILL.), és mindezek kombinációi;

gyógyászatiilag hatékony mennyiségekben, ahol a kompozíciónak van legalább egy első fázisa (A) és legalább egy második fázisa (B) az első fázis (A) által körülvéve, ahol az első fázisnak (A) van legalább egy első (a) aktív alkotórész komponense és a második fázisnak van legalább egy második (b) aktív alkotórész komponense, ahol az első fázis (A) úgy van megvalósítva, mint egy hüvely vagy burkolat (sheath), és a második fázis (B) úgy van megvalósítva, mint egy belső mag (core), ahol az első fázis (A) szilárd formában van jelen, amely feloldható szopogatás (sucking) során és/vagy a nyál befolyása alatt, és ahol a második fázis (B) folyadék formájában van jelen, ahol az (A) és (B) fázisok az (a) és (b) aktív alkotórész komponenseket kibocsátják a szopogatás során és/vagy a nyál befolyása alatt, mégpedig idő-halasztásos (time-delayed) módon, ahol az (a) első aktív alkotórész komponens időrendileg a (b) második aktív alkotórész komponens előtt bocsátódik ki a szopogatás során vagy a nyál befolyása alatt, ahol a kompozíció az (a) és/vagy (b) aktív alkotórész komponenseket egymástól függetlenül tartalmazza, mindegyiket egy mátrixban és/vagy masszában, amely cukrokon és cukor helyettesítőkon alapul, és ahol az arány, amely alapezik mind a szilárd első fázis (A) tömegén, mind a folyékony második fázis (B) tömegén, az 50-98:50-2 közti tartományban van.

2. Az 1. igénypont szerinti kompozíció, ahol a második fázis (B) viszkózus, főleg szirup-szerű, vagy akár gélszerű formában testetűl meg, elsősorban ahol a (b) második aktív alkotórész komponens és/vagy a második fázis (B) és/vagy a belső mag (core) dinamikus viszkozitása szobahőmérsékleten (20°C) és környezeti nyomáson (atmoszferikus nyomáson) az 1 mPa.s és 1000 mPa.s közötti tartományban, főleg az 5 mPa.s és 800 mPa.s közötti tartományban, előnyösen a 10 mPa.s és 500 mPa.s közötti

tartományban, még előnyösebben az 15 mPa.s és 300 mPa.s közötti tartományban, és különösen előnyösen a 20 mPa.s és 200 mPa.s közötti tartományban van.

3. Az 1. vagy 2. igénypont szerinti kompozíció, ahol az (a) első aktív alkotórész komponens alaplinktúra (elementary lincture) formájában van hozzáadva, és/vagy ahol a kivonat vizes, alkoholos vagy vizes-alkoholos kivonatra (extraktumra), előnyösen vizes-alkoholos kivonatra alapozva áll rendelkezésre, és/vagy ahol az (a) első aktív alkotórész komponens, elsősorban a cserző szer, kivonat formájában, főleg folyékony kivonat formájában, különösen alaplinktúra formájában van hozzáadva, amelyeknél a gyógyszer/kivonat arány az 1:0,5 és az 1:50 közötti tartományban, előnyösen az 1:1 és 1:20 közötti tartományban, előnyösebben az 1:5 és 1:15 közötti tartományban van.

4. Az 1-3. igénypontok bármelyike szerinti kompozíció, amely az (a) első aktív alkotórész komponensét a 0,1 tömeg % és 20 tömeg % közötti tartományban, előnyösen a 0,2 tömeg % és 10 tömeg % közötti tartományban, előnyösebben a 0,5 tömeg % és 5 tömeg % közötti tartományban tartalmazza, a gyógyászati kompozícióra alapozva.

5. Az 1-4. igénypontok bármelyike szerinti kompozíció, ahol a cserző szer muskátli (*Pelargonium*), elsősorban valamelyik dél-afrikai muskátli, mint a *Pelargonium sidoides* és/vagy a *Pelargonium reniforme*.

6. Az 1-5. igénypontok bármelyike szerinti kompozíció, ahol a (b) második aktív alkotórész komponens száraz kivonat (dry extract) formájában van hozzáadva, és/vagy ahol a kivonat vizes, alkoholos vagy vizes-alkoholos kivonatra (extraktumra), előnyösen vizes-alkoholos kivonatra alapozva áll rendelkezésre, és/vagy ahol a (b) második aktív alkotórész komponens, elsősorban nyálkaképző gyógyszer, kivonat formájában, előnyösen száraz kivonat formájában van hozzáadva, előnyösen olyan alaplinktúra formájában, amelynek gyógyszer/kivonat aránya az 1:1 és 10:1 közötti tartományban, előnyösen az 5:1 és 8:1 közötti tartományban van.

7. Az 1-6. igénypontok bármelyike szerinti kompozíció, amely a (b) második aktív alkotórész komponensét olyan mennyiségben tartalmazza, amely a 0,05 tömeg % és a 10 tömeg % közötti tartományban, előnyösen a 0,05 tömeg % és az 5 tömeg % közötti tartományban, előnyösebben a 0,08 tömeg % és a 2 tömeg % közötti tartományban van a gyógyászati kompozícióra alapozva.

8. Az 1-7. igénypontok bármelyike szerinti kompozíció, ahol a nyálkaképző gyógyszer lándzsás útifű (*buckhorn plantain*) (*Plantago lanceolata* L.).

9. Az 1-8. igénypontok bármelyike szerinti kompozíció, amely az (a) aktív alkotórész komponensét és/vagy a (b) aktív alkotórész komponensét egymástól függetlenül tartalmazza, mindegyiket egy mátrixban és/vagy masszában, ahol az (a) első aktív alkotórész komponens olyan szilárd mátrixba és/vagy masszába van beágyazva, amely feloldható szopogatás (sucking) segítségével és/vagy a nyál befolyása alatt, és/vagy ahol a (b) második aktív alkotórész komponens olyan mátrixba és/vagy masszába van beágyazva, amely feloldható a szopogatás (sucking) segítségével és/vagy a nyál befolyása alatt.

10. Az 1-9. igénypontok bármelyike szerinti kompozíció, ahol a kompozíció olyan mennyiségekben tartalmaz cukrot és/vagy cukor származékokat, amely az 50 tömeg % és 99,6 tömeg % közötti tartományban van, főleg az 60 tömeg % és 99,5 tömeg % közötti tartományban van, elsősorban a 70 tömeg % és 99 tömeg % közötti tartományban van, különösen a 80 tömeg % és 98,8 tömeg % közötti tartományban van, és legelőnyösebben a 90 tömeg % és 98,5 tömeg % közötti tartományban van, a gyógyászati kompozícióra alapozva.

11. Az 1-10. igénypontok bármelyike szerinti kompozíció, ahol az (A) első fázis, amely az (a) első aktív alkotórész komponenst tartalmazza, tartalmaz izomaltot (cukoralkoholok keveréke), elsősorban folyékony izomaltot, elsősorban 70 tömeg % és 95 tömeg % közötti mennyiségben, különösen 75 tömeg % és 90 tömeg % közötti mennyiségben, és előnyösen 80 tömeg % és 90 tömeg % közötti mennyiségben az (A) fázisra alapozva, és/vagy ahol az (A) első fázis, amely az (a) első aktív alkotórész komponenst tartalmazza, tartalmaz maltitot (egy cukoralkohol), főleg maltit szirupot, elsősorban 2 tömeg % és 20 tömeg % közötti mennyiségben, különösen 3 tömeg % és 18 tömeg % közötti mennyiségben, és előnyösen 5 tömeg % és 15 tömeg % közötti mennyiségben az (A) fázisra alapozva, és/vagy ahol a (B) második fázis, amely a (b) második aktív alkotórész komponenst tartalmazza, tartalmaz maltitot, elsősorban maltit szirupot, elsősorban 50 tömeg % és 95 tömeg % közötti mennyiségben, különösen 60 tömeg % és 90 tömeg % közötti mennyiségben, és előnyösen 70 tömeg % és 85 tömeg % közötti mennyiségben a (B) második fázisra alapozva.

12. Az 1-11. igénypontok bármelyike szerinti kompozíció, ahol az adagolási forma torok cukorka (négyzetes cukorka; lozenge), elsősorban kemény cukorka (hard candy), pasztilla vagy tableta formájában, és/vagy ahol az adagolási forma egy torok cukorkán (négyzetes cukorka, lozenge) alapul, elsősorban többfázisú, előnyösen kettős fázisú torok cukorkán (négyzetes cukorka, lozenge) alapul.

13. Az 1-12. igénypontok bármelyike szerinti kompozíció, ahol az arány a szilárd első fázis tömegére (A) és a folyékony második fázis tömegére (B) alapozva a 60-95:40-5 közti tartományban, előnyösen a 70-90:30-10 közötti tartományban van.

14. Csomagolási egység, elsősorban buborékcsoomagolás (blister package), amely tartalmazza az 1-13. igénypontok bármelyike szerinti kompozíciót, elsősorban olyan formában, amely alkalmas egyedi dózisok formájaként, előnyösen torok cukorka (négyzetes cukorka, lozenge) formájában, különösen ahol a csomagolási egység torok cukorkák (négyzetes cukorka, lozenge) sokaságát tartalmazza, főleg egyedi eltávolításhoz.

15. Alkalmazása egy, az 1-14. igénypontokban meghatározott kompozíciónak gyógyszer előállítására a száj és a torok terület gyulladásos betegségeinek, köhögésnek és a felső légúti rendszer hurutjainak helyi kezelésére.