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(54) **Title:** NASAL AND BUCCAL COMPOSITIONS FOR CONTROLLING SNORING

(54) **Titre :** COMPOSITIONS NASALE ET BUCCALE POUR LUTTER CONTRE LE RONFLEMENT

(57) **Abstract:** The invention relates to the use of a nasal composition and a buccal composition for preparing a combined composition to be used simultaneously, sequentially or separately for the treatment or prevention of snoring, especially for a person who snores heavily.

(57) **Abrégé :** La présente invention concerne l'utilisation d'une composition nasale et d'une composition buccale pour la préparation d'une composition combinée pour une utilisation simultanée, séquentielle ou séparée pour le traitement ou la prévention des ronflements chez un sujet, plus particulièrement chez un gros ronfleur.

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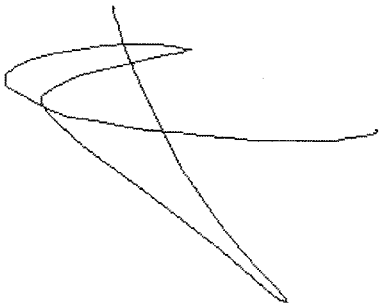

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Anti-snoring nasal and buccal compositions

The present invention relates to the field of the treatment and prevention of snoring and more particularly snoring in certain heavy snorers. In heavy snorers, a set of complex phenomena is involved which produces a characteristic snore. In these persons, the origin of the snoring is frequently pharyngeal and also nasal.

However, the targeted but not simultaneous action of some products on the pharynx and the uvula cannot completely solve the problem of some heavy snorers. In fact the problem consists in acting on phenomena that involve the anatomical structures of both the nose and pharynx. A simultaneous action on these two targets may allow better efficacy.

The general problem with snoring

Approximately 42% to 60% of adults snore from time to time; 20% of men and 10% of women snore habitually. Moderate snoring easily reaches a noise level of 45dB to 60dB (the noise of a voice) while major snoring may exceed 95dB, which corresponds to the noise of a lorry passing. In heavy snorers, the snoring often exceeds 60dB and may give rise to serious disorders, not only for the snorer himself but also for the persons who live alongside him and do not manage to sleep because of the noise. This is because sleep is often disorganised for heavy snorers and their family circle, because of the noise and intensity of the snoring

The causes of snoring vary from one person to another. On

an anatomical level, snoring mainly occurs when the respiratory tracts at the throat (pharynx) narrow after the relaxation of the muscles which normally keep the passage open. This narrowing causes a turbulent air flow and vibrations at the soft palate and at the base of the tongue, which creates the sound of the snoring. In heavy snorers, snoring of nasal origin is superimposed on snoring originating from the pharynx.

The two main causes of snoring of nasal origin are an obstruction of the nasal respiratory passages and a deformation of the nose. When the nasal passages are obstructed (nose restricted or blocked), the subject requires addition effort for breathing in. This action may create a vacuum effect in the throat and modification of the passages of the air flow at the nasal cavity that cause snoring. In addition, obstruction of the nasal passages requires the subject to breath through the mouth and is often associated with snoring coming from the throat.

Thus the appearance of snoring among heavy snorers is due to several factors that interact simultaneously with one another: principally vibrations at the pharynx and narrowing of the nasal passages.

Snoring at the pharynx

Vibrations at the pharynx are the consequence of an excessively long velum, a sleeping position in dorsal decubitus and narrowing of the buccal cavity.

The existence of an excessively long velum is the most

easily understandable factor. This hypertrophy of the velum affects the muscles of the latter relatively little but affects above all the fatty tissues that surround it, and the mucous membrane. The uvula extends, the posterior pillars of the tonsils thicken and broaden in two half-curtains extending the velum downwards.

The second factor responsible for the appearance of snoring is dorsal decubitus (the position of the sleeping body on its back). This position causes the relaxed velum to rest on the posterior wall of the pharynx. In this anatomical position, the passage of the nasal inspiratory air can easily raise it, cause it to float and vibrate. If the sleeper is lying on his stomach, the velum falls forwards and does not risk touching the posterior or even lateral wall of the pharynx; thus released it leaves wide open behind it the air passage that is behind it and the air passes easily. However, it is lying on the back that the velum best presses against the pharynx. This is the habitual position of the severe snorer and it is in this position that risks of asphyxia are the greatest.

Narrowing of the buccal cavity constitutes the third element responsible for snoring. This narrowing is caused by obesity, nasal obstruction and retrognathism.

At the pharynx, snoring represents the vibration of the soft palate and the walls of the pharynx under the action of the abnormally turbulent air flow. It is in keeping with the anatomical and mechanical characteristics of the pharynx and of the mucus, which constitute a surface viscous layer of the tissues of the pharynx. Mucus is a physiological and

anatomical element of importance since it constitutes the environment that will interact with the spray (the active agents are sprayed and must act at this level). It is therefore particularly important to note precisely the physical and physiological characteristics of this biological environment.

Between the nasal cavity and the trachea, both rigid and non-deformable, the inspiratory air will pass through a deformable space, elastic and more or less narrowed. In this narrowing modifications to the flow rate and pressure will appear, referred to as venturi phenomena, governed by Bernoulli's theorems, the origin of the vibration of the walls. Between the nasal fossae and the rigid trachea, the walls of the orohypopharynx are soft, elastic and narrowed. Everything is therefore combined for the venturi phenomenon to occur several times per second, which explains the vibration of the soft palate relating to the slapping thereof against the walls of the pharynx.

However, because of the defence reactions caused by this inspiratory discomfort, a vicious circle is created comprising an increase in the inspiratory effort under the effect of this obstruction - intended to combat the asphyxia that this causes - but responsible in its turn for an obstruction that is all the more rapid and greater, the more powerful this effort. This voluntary control being impossible during sleep, snoring as from the time when it begins can only be aggravated until awakening or semi-awakening, restoring tonus to the muscles of the oropharynx, eliminates the narrowing and its harmful effects.

For the vibration to occur, it is necessary for the soft velum, successively and approximately 30 times per minute, to touch the posterior wall of the pharynx, for it to be pushed by an air current coming from the nose, and then for any force to return it against the palate. In deliberate snoring, this force is the intentional contraction. In passive nocturnal snoring in the prone position, this force is that of gravity, and when it is applied to a long voluminous velum, the latter tends spontaneously to stick to the pharynx.

Snoring at the nasal level

Snoring of nasal origin is the consequence of a narrowing of the nasal passages. The more the tissues relax or the more difficult is the air passage, then the risk of snoring is great. Audible respiration may be caused or accentuated by polyps in the nasal passages (a polyp is slender growth that occurs on a mucous membrane); a congestion of the nasal passages (cold, allergy, absorption of alcohol or tranquilisers) and relaxation of the tissues with age.

The nasal cavity is bordered by a pseudo-stratified epithelium that rests on a basal membrane, separating it from the deep sub-mucous layers. The sub-mucous layers are composed of mucus, seromucus and serous glands. The local blood flow is distributed to the cells by virtue of a network of small arteries, arterioles and arterio-venous anastomoses. The vascular capacitance, formed by the veins and cavernous sinusoids, determines the degree of opening of the nasal passages. The contraction or relaxation of this set of vessels is under the influence of the sympathetic

system. The cavernous sinusoids are more dense than the inferior and middle conchas and are composed of smooth muscular cells controlled by the sympathetic nervous system. A loss of sympathetic tonus, or to a lesser degree a cholinergic stimulation, cause an engorgement of this erectile sinusoidal tissue.

The opening of the nasal passages is controlled mainly by the changes that occur in the capacitance of the vessels. The resistance of the superior nasal passages is in fact responsible for two thirds of the total resistance to air of the respiratory passages. The predominant sites of nasal obstruction to the passage of air are the nasal vestibule, the nasal valves and the nasal conchas.

There exist physiological variations in the opening of the nasal passages, known by the term "nasal cycle". The main consequence of these variations is change in capacitance of the blood vessels situated in the inferior and middle conchas. These changes alternate from one nasal cavity to the other approximately every two to four hours in 70% of persons. Posture also intervenes in the regulation of the degree of vascular congestion. The nasal obstruction increases bilaterally when the subject places himself in a supine position, and increases unilaterally according to the lateral position of the subject.

The nasal origin of snoring is an increase in the resistance to the passage of air of the superior nasal passages, more precisely at the nasal valve and inferior and middle conchas. This is the result of a physiopathological congestion mechanism, resulting in a dilation of the blood

vessels, an increased mucus secretion, and a dilation of the smooth muscular structures. The resistance to the passage of air increases and modifies the air flows causing vibrations of the soft tissues of the palate and uvula.

In heavy snorers

It appears that, in heavy snorers, the physiological changes found at the nasal passages and at the pharynx produce characteristic snores, which are not found in snorers where the origin of the snoring is either nasal or at the pharynx. The snores of heavy snorers are characterised in fact by a particular frequency and intensity.

Snores in a "standard" snorer have a frequency between 200 and 2000 Hz, with decibel levels ranging up to 70 dB. The frequency varies according to the origin of the snores [Perez-Padilla JR, Skawinski E, Difrancesco LM, Feige RR, Remmers JE, Whitelaw WA. Characteristics of the snoring noise in patients with and without occlusive sleep apnoea. Am Rev Respir Dis. 1993 Mar; 147(3):635-441]. The snores of heavy snorers may be fairly powerful in intensity. The average subject has a snore of between 40 and 50 dB, with subjects ranging up to 80-90 dB and sometimes even 105 dB. It seems that snoring of nasal origin has a lower intensity than snoring of buccal origin. In certain heavy snorers, the intensity of the snoring is such that it causes hearing problems in their partners.

Scientific studies were carried out so as to specify in more detail, in heavy snorers, whether there existed changes to the cavity of the pharynx, or variations in intensity and

passage of the inspired and expired air flows. By virtue of these data, the company Persee Medica was able to show what was the relationship between nasal and buccal causes of snoring in heavy snorers.

Green et al show in a study on 18 volunteers, distributed in two groups depending on whether they snored or not, that the volume of the cavity of the pharynx is not different from one group to another [Green DE, Block AJ, Collop NA, Hellard DW. Pharyngeal volume in asymptomatic snorers compared with nonsnoring volunteers. Chest. 1991 Jan;99(1):49-53]. This element is therefore not a distinguishing element in heavy snorers.

The intensity and frequency of snoring are distinguishing characteristics. This is because snores of nasal and buccal origin have different intensities and different frequencies. In heavy snorers, there is a superimposition of the different intensities for the same frequency and addition of intensities at different frequencies, which gives this aspect of diffuse noise over the recording spectra.

Stanescu and his team show that heavy snorers have problems with limitation of the inspired and expired air [Stanescu D, Kostianev S, Sanna A, Liistro G, Veriter C. Expiratory flow limitation during sleep in heavy snorers and obstructive sleep apnoea patients. Eur Respir J 1996 Oct; 9(10):2116-21].

All the changes and disturbances that occur in heavy snorers give rise to a modification to the air flows at the buccal and nasal levels producing very heavy snoring, very

characteristic in terms of frequency, intensity and profile of the recording spectrum.

Heavy snorers have simultaneously modifications to the air flows at the nose as well as vibration of the soft palate. These phenomena are not independent of each other but on the contrary strongly correlated.

The vibration of the soft palate takes place mainly under the influence of the air flows coming from the nasal passages (often increased following respiratory difficulty). This vibration is itself maintained by a reduction in the tonicity of the muscles of the pharynx and the uvula and produces a local inflammation which in its turn increases the atony. A first "vicious circle" sets up and thus maintains the snoring phenomenon. Likewise, the vibration of the soft palate causes disturbances to the passage of the air during inspiration and expiration and consequently an increase in the respiratory effort at the nasal passages. This maintains a localised inflammation and congestion and thus reinforces the phenomenon. There is thus present a second "vicious circle" that reinforces the phenomena giving rise to snoring in heavy snorers.

This interleaving of several imbalances produces snoring of very great intensity and frequency characteristic of heavy snorers [see appended figure].

Prior art

The products marketed against snoring are preparations based on oils for lubricating the mucosa of the pharynx or nasal

mucosa. These products are often perceived as ineffective by a great majority of consumers. This is because it is often mentioned that these products act rapidly but lose their efficacy in the first hour of sleep, a short time after application.

This finding is explained by the fact that these products do not remain in place on their site of action and are rapidly eliminated towards the back of the throat (mouth sprays). This is because the velocity of the mucus and the influence of the constant salivatory flow cause an elimination of the oily products with the main consequence of a short duration of action.

Some products contain essential oils. The essential oils used in these preparations are not, with regard to some of them, devoid of toxicity. Some essential oils are in fact the subject of restrictions on use and warnings following the revealing of their toxicity signalled by pharmacovigilance investigations.

In addition, the spraying of oily preparations in the pharynx and nose is associated with risk of oil pneumopathies, because of the passage of lipidic droplets in the lungs. Faced with the appearance in France of a few cases of oily pneumopathies following the administration of anti-snoring products containing oils, the French health authorities (AFSSAPS) have informed the manufacturers of the products involved of their preoccupation and have requested additional data on the safety of these products. The risk of passage at a pulmonary level of the oils contained in these preparations represents in fact a certain risk for the

safety of the consumer.

Finally, the does not exist any product allowing simultaneous action on the nasal and buccal origins of snoring.

Description of the invention

The research work carried out by the applicant have made it possible to develop a new strategy for the treatment and prevention of snoring particularly suited to heavy snorers. This is because the interaction between nasal snoring and snoring whose origin is the pharynx (uvula) and the interleaving between these two phenomena have the consequence of producing a higher noise level of snoring.

In the case of snoring in heavy snorers, this necessarily involves the setting up of simultaneous treatment of these two different targets.

This aim is achieved according to the invention by virtue of the use of a nasal composition and a buccal composition for the preparation of a combined composition for simultaneous use, sequential or separate, for the treatment or prevention of snoring in a subject, in particular in a heavy snorer. This association can be presented grouped in the same offer, or separated by two individual offers grouped together in any form.

The nasal composition is preferably in the form of a nasal spray comprising:

- a first substance or combination of substances providing a

decongestioning action in order to increase the nasal lumen by an action of the sympathetic type on the smooth muscles, an action of vasoconstriction of the blood vessels and a local anti-inflammatory action in order to reduce the exaggerated secretion of mucus and vasodilatory substances;

- a second substance or combination of substances providing a reduction of the resistance of the air at the nasal valve and middle and inferior conchas by the formation of a "sliding area" and the lubrication of the tissues of the nasal passages;

- a third substance or combination of substances having bio-adhesiveness properties and making it possible to keep the first and second substances at their action site.

The first substance or combination of substances is chosen from the group comprising an extract of *Ruscus aculeatus* and rutin.

The second substance or combination of substances is chosen from the group comprising sea water, glycerine and phosphatidylcholine.

The third substance or combination of substances is chosen from the carrageenan group.

The extract of *Ruscus aculeatus* aims to cause an action of vasoconstriction of the blood vessels in the form of an action of the adrenergic type on the smooth muscles of the walls of the vessels and to increase the nasal lumen and consequently to reduce the resistance to the passage of air in the nasal passages. During a trial published in 2000

relating to 148 subjects monitored during 12 weeks, an extract of *Ruscus aculeatus* proved to be more effective than a placebo for relieving the symptoms of chronic venous insufficiency by causing a vasoconstriction of the vein walls [Lucker P, Jost V, Wolna P, et al. Efficacy and safety of ruscus extract compared to placebo in patients suffering from chronic venous insufficiency. Phytomedicine. 2000;7(suppl 2):P-155].

Rutin makes it possible to initiate a local anti-inflammatory action in order to reduce exaggerated secretion of mucus and vasodilatory substances, so as to reduce oedema, vasodilation following inflammation and relaxation of the tissue structures of the smooth muscles and consequently to allow an increase in the nasal lumen. Rutin forms part of the large family of bioflavonoids. It is chemically very close to quercetin (another flavonoid) and possesses antioxidant, anti-inflammatory, vasoprotective (protection of the blood vessels) and anti-thrombotic (protection against the formation of blood clots) properties. Rutin is present in several medicinal plants, including eucalyptus, hawthorn, ginkgo biloba and St John's wort.

Experiments have been carried out in animals. They show that the anti-inflammatory activity of rutin is more pronounced during chronic inflammation than other compounds such as quercitin and hesperidin [Giardia T, Rottelli AE, Juarex AO, Pelzer LE. Anti-inflammatory properties of plant flavonoids. Effects of rutin, quercetin and hesperidin on adjuvant arthritis in rat. Farmaco. 2001 Sep;56(9):683-7].

Glycerine and phosphatidylcholine provide lubrication functions. Sea water makes it possible to obtain a "sliding area" facilitating the passage of air at the nasal passages by reducing the resistance mechanisms. Sea water has many therapeutic virtues and mainly by internal local route, particularly in nasal ailments. The local installation of a physiological solution of sea water affords a reduction in inflammation of the nasal mucus and the obtaining of a "sliding area". Sea water contains numerous mineral salts and oligoelements that restore the ciliate functions of the mucus.

The nasal composition of the invention is remarkable in that it offers properties of lubrication of the nasal mucosa and pharynx over a long period by virtue of the carrageenans, which have bioadhesive properties on the mucosa.

All these substances enable the nasal spray to reduce the air resistance at the nasal passages. This reduction consequently cause a reduction in the turbulence of the air flows at the pharynx caused by the increase in the buccal respiration.

In the nasal composition of the invention, and by virtue of the first substance or combination of substance:

- the ruscus extract, if present, represents around 0.01 to 5% or around 0.03 to 0.07% and preferably around 0.5% by weight of the composition,

- rutin, if present, represents around 0.01 to 0.05% and preferably around 0.15% by weight of the composition,

at least one of the above substances being present in the composition.

In the nasal composition of the invention, and by virtue of the second substance or combination of substances:

- sea water, if present, represents around 0.1 to 10% or around 0.5 to 5% and preferably around 1% by weight of the composition,

- glycerine, if present, represents around 1 to 10% or around 1 to 4% and preferably around 2.65% by weight of the composition,

- phosphatidylcholin, if present, represents around 0.5 to 10% or around 0.5 to 2.5% and preferably around 1.66% by weight of the composition,

at least one of the above substances being present in the composition.

In particular, the composition comprises a ratio by weight of the second substance to the first substance ranging from 20 to 100, in particular from 30 to 80, or even from 40 to 70.

In the nasal composition of the invention and by virtue of the third substance or combination of substances, the carrageenans represent around 0.5 to 2% and preferably around 1% of the composition.

The composition can comprise a ratio by weight of the third substance to the first substance ranging from 1 to 50, in

particular from 2 to 20, or even 5 to 15.

The composition can comprise a ratio by weight of the second substance to the third substance ranging from 1 to 50, in particular from 2 to 20, or even 3 to 10.

The invention concerns the association of the above nasal composition with a buccal composition in the form of a mouth spray. Thus the invention relates to a method for treating or preventing snoring in a subject consisting of the said subject receiving a combination of an aforementioned nasal composition with a buccal composition in the form of a mouth spray.

Thus the invention relates to the use of a nasal composition as defined previously for the treatment or prevention of snoring in a subject, in particular in a heavy snorer, the said nasal composition being received by the said subject in combination with a buccal composition against snoring.

The buccal composition comprises at least one lubricating substance and at least one bio-adhesive substance able to make the said lubricating substance adhere to the mucocilliary cells situated at the pharynx. The bio-adhesive substance is chosen from the group comprising polysaccharides, cellulose derivatives, acrylic derivatives or protein derivatives. Preferably the bio-adhesive substance is a polysaccharide belonging to the family of carrageenans.

The buccal composition comprises approximately 0.5 to 20% bio-adhesive substance, and in particular carrageenans.

This composition contains approximately 1 to 5% and preferably approximately 1.5 to 3% bio-adhesive substance, and in particular carrageenans. It can also contain approximately 5 to 20%, and approximately 10 to 15% bio-adhesive substance, and in particular carrageenans.

In the buccal composition, the lubrication substance is a surfactant having a polar part and a hydrophobic part. The polar part of the surfactant is chosen from the group comprising glucose, sucrose, lactose, glycerol, xylose, peptides, amino acids and nucleotides. The hydrophobic part is chosen from the group comprising fatty acids, a fatty alcohol, a fatty amine, esters, glycerides and phospholipids. The hydrophobic part consists of phospholipids, for example phosphatidylcholine.

This buccal composition contains approximately 0.5 to 20% lubricating substance, and in particular phosphatidylcholine. It may preferably contain approximately 2 to 10% lubricating substance, and in particular phosphatidylcholine.

This buccal composition also comprises one or more anti-inflammatory and/or tonic agents for the mucous membranes and tissues of the pharynx.

The tonic agent for the mucous membranes and the tissues of the pharynx is rosehip. The buccal composition contains between 0.01 and 5% tonic agent, and in particular rosehip.

The buccal composition is in the form of an aerosol, more especially a foam.

A preferred buccal composition contains:

- approximately 1 to 5%, and preferably approximately 3%, carrageenans;

- approximately 1 to 10%, and preferably approximately 5%, phosphatidylcholine;

- approximately 0.01 to 5%, and preferably approximately 2%, rose hip.

The composition of the buccal spray makes it possible to lubricate the walls of the pharynx (the uvula) and to increase the tonicity of the smooth muscular structures throughout the night by virtue of the bio-adhesive action of the carrageenans. The nasal spray reduces nasal congestion, reduces chronic inflammation and lubricates the walls in order to facilitate the passage of the air flows during inspiration and expiration.

The research work carried out by the applicant enabled it to reveal a synergy between carrageenans and glycerine. This is because the bio-adhesion properties of carrageenans are significantly enhanced by glycerine.

The invention proposes the use both in the nasal composition and in the buccal composition of two important agents, carrageenans and glycerine. Carrageenans are used for their bio-adhesion properties. Glycerine emulsifies and thus disperses phosphotidylcholine, which is a lubricating agent with a lipophilic character, in the end composition with a hydrophilic character.

Carrageenans have bio-adhesion properties. Glycerine on the other hand has no bio-adhesion property. Glycerine is an agent that is found in a multitude of pharmaceutical preparations. This texturising agent is not described in the literature as a bio-adhesive agent. Glycerine generates in the composition a moderate increase in viscosity.

However, surprisingly, the applicant, by virtue of several experiments, discovered that glycerine greatly increased the bio-adhesion of carrageenans. This is because glycerine increases the bio-adhesiveness factors of the preparation even when the latter are corrected for the influence of viscosity. Thus, in the presence of glycerine, the corrected adhesion-suitability factor is multiplied by 200 and the bio-adhesiveness factor is increased by 100%. As mentioned previously, glycerine does not have any bio-adhesion properties. However, these experiments demonstrate that it fulfils a synergy role with carrageenans in order to greatly increase their bio-adhesive properties.

This property also applies to other bio-adhesive agents of any type, in particular agents such as carbopols and the other derivatives of cellulose. This is because carrageenans have many groups facilitating the formation of hydrogen bonds in the presence of water or molecules having hydrophilic groups. These groups are hydroxyls (-OH), present on galactose molecules, the base unit of the polysaccharide polymer, that carrageenans constitute. These structural properties have similarities with many other bio-adhesive compounds such as carbopols for example. Carbopols are cross-linked polymers of acrylic acid. By studying the

similarities in structures between carrageenans and carbopols, it is possible to conclude that these substances and derivatives will increase the bio-adhesion properties of carrageenans.

The invention also concerns a pack or case, or a set, comprising the two previous compositions so as to associate the two combined action modes in any form, as well as instructions for use so as to offer the subject afflicted with snoring a treatment based on their combined action making it possible to attack simultaneously the two causes of the noise caused in heavy snorers. The two products that make up this case or pack can be used in a precise order or on the contrary not in any order.

The compositions making up this pack can be packaged in a container comprising several chambers, or in separate containers. The containers may be packaged in a single package. The pack may be in duo or mixed form or a twin presentation. Thus pack also means any packaging where the two compositions are associated, consisting of cardboard, paper, transparent coloured plastic, possibly of different colours, sizes or even materials etc.

This combination of compositions for the first time makes it possible to treat interactions between the nasal and pharyngeal physiological changes giving rise to snoring in heavy snorers. This is because several "vicious circles" are set up, which start progressively, reinforced by episodes of obstruction of the upper respiratory tracts which cause modifications to the air flows. Only the combination of the technical solutions afforded by the

invention make it possible to act simultaneously on the causes of snoring in order to significantly reduce or even eliminate the noise of snoring in heavy snorers.

In the present invention, unless indicated to the contrary, the % are % by weight with respect to the total weight of the composition.

Other characteristics of the invention will emerge from the examples of nasal and buccal compositions that follow.

Heavy Snorer nasal composition (nasal spray) [qs: quantity sufficient for]

Ingredients	Dosage in end product	Range
Carrageenans	1%	0.1 - 10%
Phosphatidylcholine	1.66%	0.5 - 10%
Sea water	1%	0.1 - 10%
Ruscus (extract of Ruscus aculeatus)	0.5%	0.01 - 5%
Rutin	0.15%	0.01 - 5%
Glycerine	2.65%	1 - 10%
Additives,	/	/

preservatives and flavourings		
Water	qs 100%	qs 100%

Buccal composition (throat spray) [qs: quantity sufficient for]

Ingredients	Dosage in end product	Ranges
Carrageenans	3%	1 - 20%
Phosphatidylcholine	5%	1 - 10%
Meadowsweet (extract of *Filipendula ulmaria)*	3%	1 - 5%
Rosehip (extract of *Rosa canina*)	0.3%	0.01 - 5%
Glycerine	8%	1 - 20%
Additives, preservatives and flavourings	/	/
Water	qs 100%	qs 100%

Other advantages and characteristics of the invention will emerge from the following examples, in which reference will be made to the accompanying figures, in which:

- figure 1 shows the curves of the recordings and reference curve for snoring persons taking no product,

- figure 2 shows the curves of the recordings and the reference curve for snoring persons taking SILENCE Throat,

- figure 3 shows the curves of the recording and the reference curve for snoring persons taking SILENCE Heavy Snorers,

- figure 4 shows the curves of the recordings and the reference curve for snoring persons,

- figure 5 shows the reduction in the duration of the snoring according to the use or not of the product.

I - Description of the compositions

The following compositions were used in the experiments reported below.

- Silence Heavy Snorers mouth spray: lubricating agents (including phosphatidylcholine), bio-adhesive agents and bio-adhesion reinforcement agents (carrageenans and glycerine), mucous membrane toning agents and technological excipients.

- Silence Heavy Snorers nasal spray: agents promoting the

passage of air (lubricant, vasoconstrictor, decongestant), bio-adhesive agents and bio-adhesion reinforcement agents (carrageenans and glycerine), technological excipients.

- SilentNight mouth spray: lubricating agents, technological excipients.

II - Methodology

1) Study of the background noise in a bedroom. The objective was to have a reference for evaluating the noise level in a bedroom occupied by a couple of non-snorers and to consider this noise as a background noise, that is to say a noise inherent in respiration and the movement of sleeping persons. It should be remarked that this background noise is extremely sensitive to the environment, depending on the situation of the apartment or house in an urban or rural environment. In this investigation, a certain number of prior conditions had to be fulfilled, and in particular a "calm" situation in the bedroom, a bedroom protected by double glazing, the door of which remained closed throughout the night. In addition, the grouping together of measurements by the calculation of means makes it possible to exclude interference caused by temporary external influences (a car passing in the street), which constitute a significant increase in decibels over a short period and thereby act very little in the calculation of the mean.

2) Study of the noise generated by a couple of one or two snorers. The objective was to evaluate the noise generated by the snorer when the latter is using no product. The new Silence product having to allow a significant noise

reduction in comparison to this sound level. In this precise case, the two persons sharing the bedroom took one of the products or not, according to the operating protocol.

3) Study of the noise generated by a pair of one or two snorers using Silence Throat. The objective was to evaluate the gains in noise level obtained by the product Silence Throat.

4) Study of the noise generated by a pair of one or two snorers using the Silence Throat and Silence Heavy Snorers product. The final objective was to measure the performance obtained by the various products and to compare them. The study also analysed a product present on the market called SilentNight. This product is sold in the form of a throat spray, a nasal spray and strips to be applied to the tongue.

The recordings were carried out throughout the night, from 11 pm to 5 am. Only the period from 1 am to 3 am was adopted for analysing the noise. The software of the equipment makes it possible in fact to produce from a recording an analysis report comprising the following data: mean of the recording and median, snoring period (> 55 dB), duration of the recording and duration of analysis of the interval, and finally, for each intensity level ranging from 99 dB to 36 dB (in decreases of 3 dB), the percentage of the interval greater than this intensity value. The products used were Silence Throat and Silence Heavy Snorers.

III - Results

The curves presented in the accompanying figures indicate on

the x-axis the various measurement levels (for example > 45 dB, > 48 dB, etc) and the y-axis indicates the percentage of the interval measured for each measuring level. The recordings show that the sound level intensity mean in a room containing two non-snoring persons indicates a level of between 42 dB and 45 dB. In a couple of snorers, the chopping according to the intensity of the different nights recorded makes it possible to establish a reference curve. The objective of this reference curve is to be able to make a comparison with similar curves during the use of Silence Throat and Silence Heavy Snorers. The reference curve is formed from means of the values considered for each measurement level. Figure 1 presents the different recording curves and the reference curve.

The recording curves and the reference curve for snoring persons taking Silence Throat and Silence Heavy Snorers are respectively presented in figures 2 and 3.

The results obtained by the equipment can be used and make it possible to produce curves from the recordings of the decibel levels throughout the night and over an interval of two hours. The recordings were carried out at a frequency of 1200 Hz. The interval of two hours is between 1 am and 3 am. The recordings show that the sound level intensity mean in a room containing two non-snoring persons indicates a level of between 42 dB and 45 dB. This level is higher than the level found during a previous experiment (36 to 39 dB). This is explained by the geographical location of this test, the apartment being situated in an urban environment (more noisy than a rural environment) although benefitting however

from the conditions required prior to the experiment (double glazing etc). It should also be noted that, with a mean of 45 dB for an environment of non-snoring persons, this is at the limit of audibility described by the Fletcher-Munson curves. This value influences the analyses of the recording curves for persons taking the product or not. So as to eliminate in the analysis the noises resulting from the ambient environment and the persons present in the room, it is agreed to choose as a lower limit a recording level of 48 dB. In addition, the recordings show that, beyond 75 dB, there is no longer any recording of sounds. Thus the analysis range is defined between 75 and 48 dB. The three reference curves (no product - Silence Throat - Silence Heavy Snorers) have been placed on the same curve (figure 4).

It can be seen in figure 4 that, over an interval of two hours (1 am to 3 am), the snoring (intensity greater that 48 dB) in a couple of snorers taking no product concern 12% of the interval, that is to say approximately 15 minutes. In persons using Silence Throat, the duration of the snoring represents no more than 9% (10 minutes), that is to say a drop of 30%. Finally, still with respect to the reference curve, in a couple using Silence Heavy Snorers, this duration is reduced to 6% of the interval, that is to say 6 minutes. In the latter case, the reduction is 50%. Compared with Silence Throat, the reduction is 22%.

These results show the great efficacy of the products Silence Throat and Silence Heavy Snorers. They confirm the need to use Silence Heavy Snorers in persons having snoring

of nasal and buccal origin and confirm the increase in efficacy by the simultaneous use of two products. This is because, without taking a product, the duration of the snoring during a night may in some people reach more than 2 hours.

Figure 5 presents the reduction in the duration of the snoring according to the use or not of the products Silence Throat or Silence Heavy Snorers, compared with the reference curve (no product).

The Student tests show that Silence Throat and Silence Heavy Snorers present a reduction in the intensity of the snoring that is statistically significant compared with the reference ($p<0.05$).

CLAIMS

1. Use of a nasal composition and buccal composition for preparing a combined composition for simultaneous, sequential or separate use for the treatment or prevention of snoring in a subject, more particularly in a heavy snorer.

2. Use according to claim 1, characterised in that the nasal composition comprises:

- a first substance or combination of substances providing a decongestioning action in order to increase the nasal lumen by an action of the sympathetic type on the smooth muscles, an action of vasoconstriction of the blood vessels and a local anti-inflammatory action in order to reduce the exaggerated secretion of mucus and vasodilatory substances;

- a second substance or combination of substances providing a reduction of the resistance of the air at the nasal valve and middle and inferior nasal conchas by the formation of a "sliding area" and the lubrication of the tissues of the nasal passages;

- a third substance or combination of substances having bio-adhesive properties and making it possible to keep the first and second substances at their action site.

3. Use according to claim 2, characterised in that the first substance or combination of substances is chosen from the group comprising an extract of *Ruscus aculeatus* and

rutin.

4. Use according to claim 2 or 3, characterised in that the second substance or combination of substances is chosen from the group comprising sea water, glycerine and phosphatidylcholine.

5. Use according to any one of claims 2 to 4, characterised in that the third substance or combination of substances is chosen from the carrageenan group.

6. Use according to any one of claims 2 to 5, characterised in that:

- the ruscus extract, if present, represents around 0.01 to 5% and preferably around 0.50% by weight of the composition,

- rutin, if present, represents around 0.01 to 5% and preferably around 0.15% by weight of the composition,

at least one of the above substances being present in the composition.

7. Use according to any one of claims 2 to 6, characterised in that:

- sea water, if present, represents around 0.1 to 10% and preferably around 1% by weight of the composition,

- glycerine, if present, represents around 1 to 10% and preferably around 2.65% by weight of the composition,

- phosphatidylcholine, if present, represents around 0.5 to 10% and preferably around 1.66% by weight of the

composition,

at least one of the above substances being present in the composition.

8. Use according to any one of claims 2 to 7, characterised in that carrageenans represent around 0.1 to 10% and preferably around 1% of the nasal composition.

9. Use according to any one of the preceding claims, characterised in that it is in the form of a nasal spray.

10. Use according to any one of the preceding claims, characterised in that the buccal composition against snoring comprises at least one lubricating substance and at least one bio-adhesive substance able to make the said lubricating substance adhere to the mucocilliary cells situated at the pharynx.

11. Use according to claim 10, characterised in that the bio-adhesive substance is chosen from the group comprising polysaccharides, cellulose derivatives, acrylic derivatives and protein derivatives.

12. Use according to claim 11, characterised in that the bio-adhesive substance is a polysaccharide belonging to the carrageenan family.

13. Use according to any one of claims 10 to 12, characterised in that the buccal composition contains approximately 0.5 to 20% bio-adhesive substance, and in particular carrageenans.

14. Use according to claim 13, characterised in that the buccal composition contains approximately 1 to 5% and preferably approximately 1.5 to 3% bio-adhesive substance, and in particular carrageenans.

15. Use according to claim 13, characterised in that the buccal composition contains approximately 5 to 20% and approximately 10 to 15% of bio-adhesive substance, and in particular carrageenans.

16. Use according to any one of claims 10 to 15, characterised in that the lubricating substance is a surfactant having a polar part and a hydrophobic part.

17. Use according to claim 16, characterised in that the polar part of the surfactant is chosen from the group comprising glucose, sucrose, lactose, glycerol, xylose, peptides, amino acids and nucleotides.

18. Use according to claim 16, characterised in that the hydrophobic part is chosen from the group comprising fatty acids, a fatty alcohol, a fatty amine, esters, glycerides and phospholipids.

19. Use according to claim 18, characterised in that the hydrophobic part consists of phospholipids, for example phosphotidylcholine.

20. Use according to any one of claims 10 to 19, characterised in that the buccal composition contains approximately 0.5 to 20% lubricating substance, and in particular phosphatidylcholine.

21. Use according to claim 20, characterised in that the buccal composition preferably contains approximately 2 to 10% lubricating substance, and in particular phosphatidylcholine.

22. Use according to any one of claims 10 to 21, characterised in that the buccal composition also comprises one or more anti-inflammatory and/or tonic agents for the mucosa and tissue of the pharynx.

23. Use according to claim 22, characterised in that the tonic agent for the mucosa and tissue of the pharynx is rose hip.

24. Use according to claim 22 or claim 23, characterised in that the buccal composition contains between 0.5 and 5% tonic agent, and in particular rose hip.

25. Use according to any one of claims 10 to 17, characterised in that the buccal composition is in the form of a foam.

26. A pack comprising at least one nasal composition and at least one buccal composition, for the treatment or prevention of snoring in a subject, more particularly in a heavy snorer, and instructions for use.

27. A pack according to claim 26, characterised in that it comprises at least one nasal composition as defined in any one of claims 2 to 9 and at least one buccal composition as defined in any one of claims 10 to 25.

Figure 1

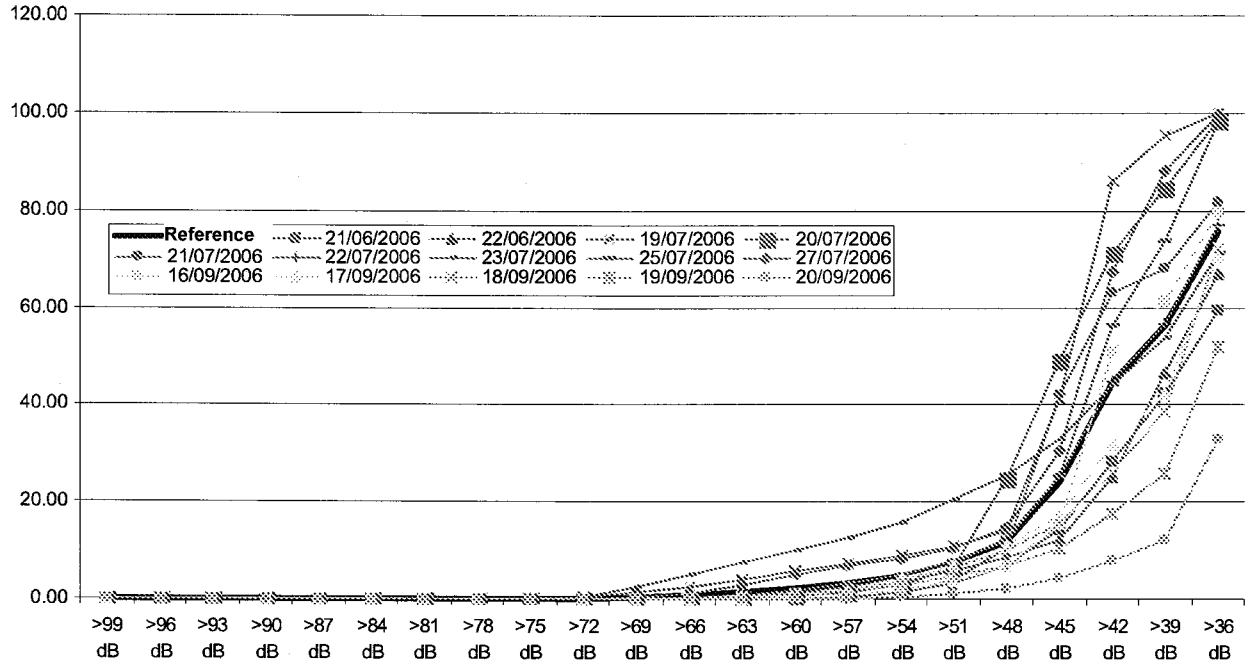


Figure 2

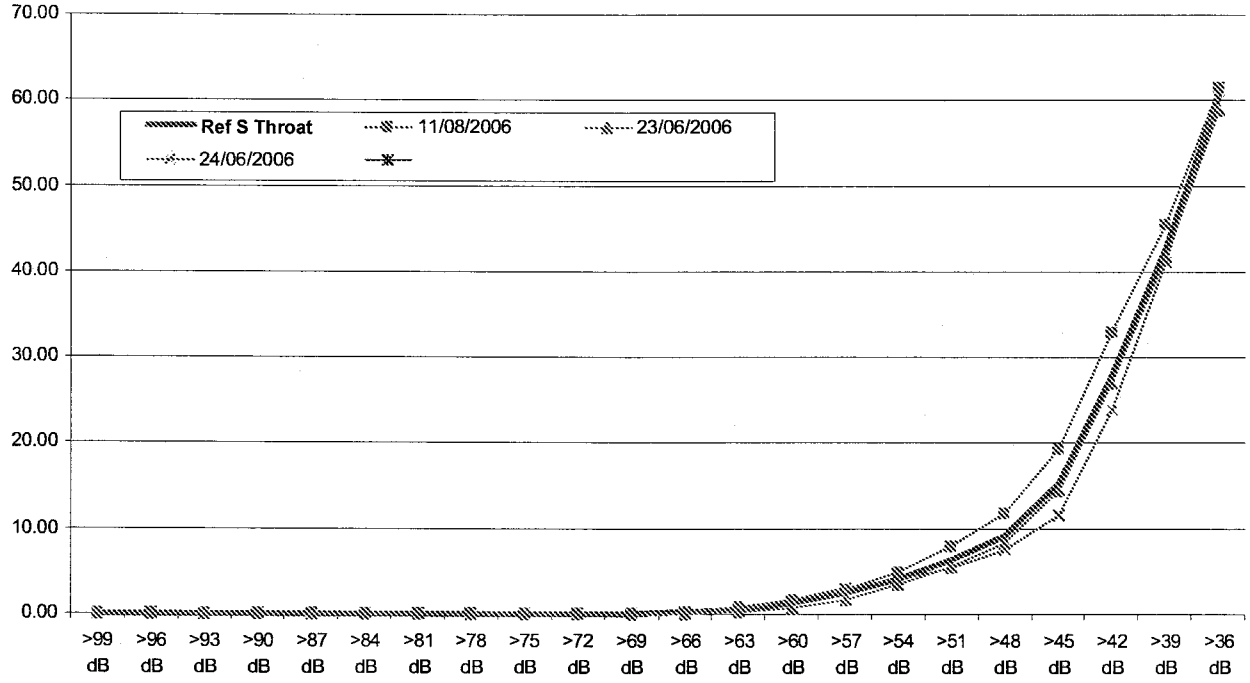


Figure 3

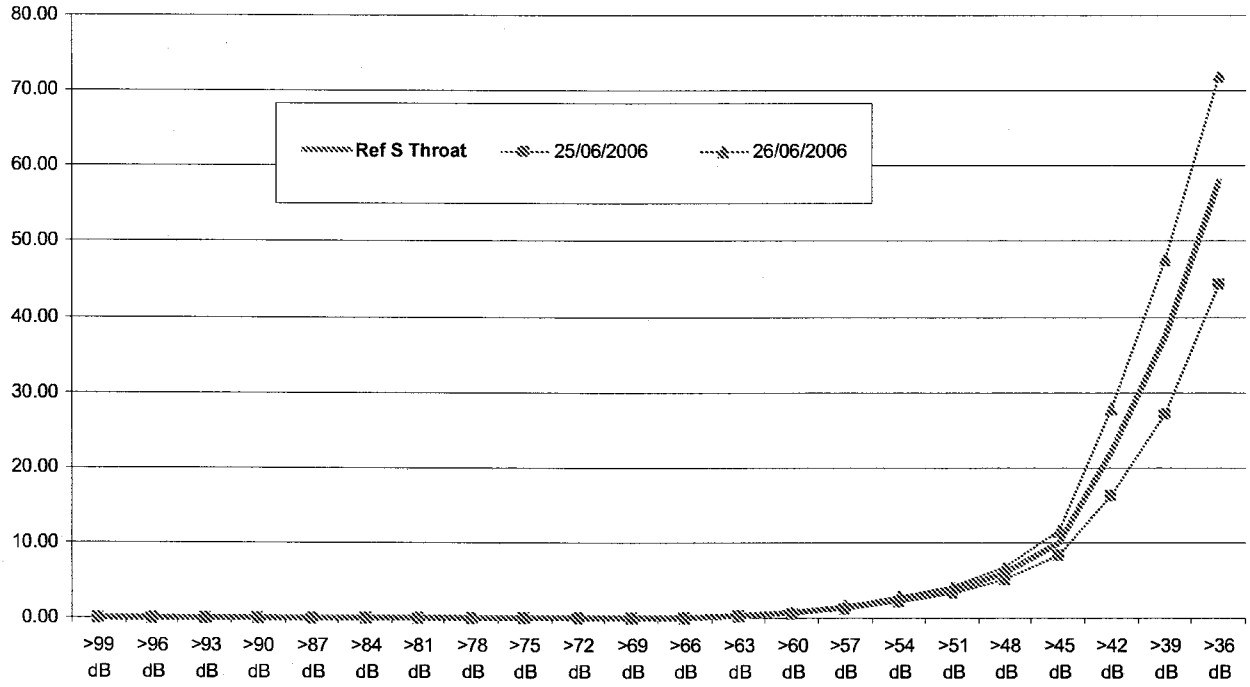


Figure 4

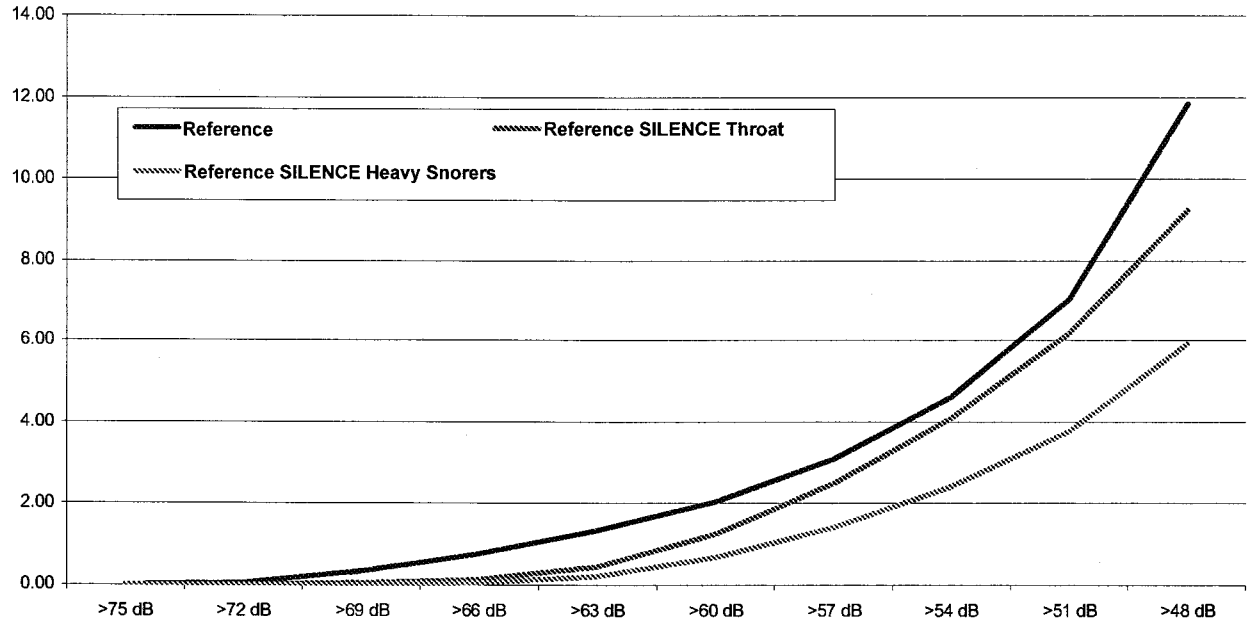
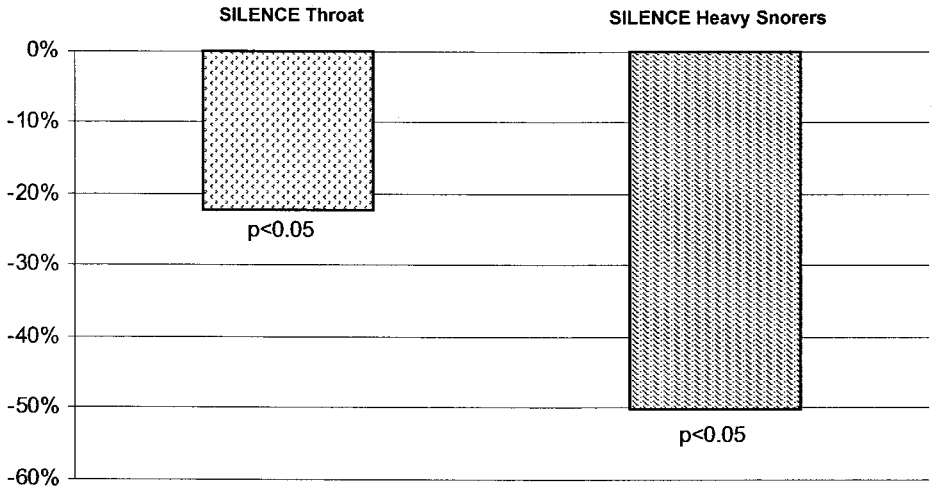


Figure 5


SILENCE Throat
SILENCE Heavy Snorers
0%
-10%
-20%
-30%
-40%
-50%
-60%
p<0.05
p<0.05