

Lip Enhancement compositions

The present invention relates to cosmetic kits and components therefor as well as to a method of topical cosmetic treatment using such kits for the emphasis of the lips.

Full, red lips are seen as a sign of youth and health. As the body grows older, the lips naturally fade and shrink slightly. Thus for centuries efforts have been made to recapture the effect of youth by colouring the lips, e.g. with lipsticks or lip glosses, or more recently by local injection or implantation of natural or synthetic materials to produce lip enlargement.

Lip glosses and lipsticks however have two significant drawbacks - the first is a drying of the lips which is uncomfortable to the wearer - the second is the tendency for lip contact to stain fabrics or leave smears on the skin. Injections or implants involve the services of a physician, are expensive, painful, non-reversible, and sometimes the effect achieved is not precisely that desired by the patient.

There is thus an ongoing need for cosmetics which can achieve the effect of emphasizing the lips and which can be self-applied.

We now propose a cosmetic kit comprising a first composition containing a vasodilator for application to the lip surface and a second composition containing a vasoconstrictor for application to the periphery of the lips; the combined effect of the two compositions is to emphasize the lips by swelling the body of the lips while tightening the skin around the rim of the lips.

Thus viewed from one aspect the invention provides a

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cosmetic kit comprising: a first topical cosmetic composition comprising a physiologically tolerable vasodilator and at least one cosmetic carrier or excipient; a second topical cosmetic composition comprising a physiologically tolerable vasoconstrictor and at least one cosmetic carrier or excipient; optionally instructions for the application of said compositions to the lips and lip periphery; and optionally a container or support for said compositions.

Viewed from a further aspect the invention also provides a topical cosmetic composition comprising a physiologically tolerable vasodilator and at least one cosmetic carrier or excipient, and instructions for the application of said composition to the surface of the lips in conjunction with the application to the periphery of the lips of a further topical cosmetic composition comprising a physiologically tolerable vasoconstrictor.

Viewed from a still further aspect the invention provides a topical cosmetic composition comprising a physiologically tolerable vasoconstrictor and at least one cosmetic carrier or excipient, instructions for the application of said composition to the periphery of the lips in conjunction with the application to the surface of the lips of a further topical cosmetic composition comprising a physiologically tolerable vasodilator.

Viewed from a yet further aspect the invention provides a method of cosmetic treatment to emphasize the lips, said method comprising applying to the surface of the lips an effective amount of a physiologically tolerable vasodilator and applying to the periphery of the lips an effective amount of a physiologically tolerable vasoconstrictor.

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The vasodilator used according to the invention may be a natural or synthetic material and may be a drug substance or a naturally occurring material, e.g. a plant extract or fragment. Most preferably it is a natural plant extract or fragment (e.g. powdered plant material). The use of natural materials in cosmetics, especially materials which occur naturally in foodstuffs, is particularly preferred as animal testing may be avoided and as customer acceptability is high. Examples of natural vasodilators include Astragalus (*Astragalus membranaceus*), Cayenne (*Capsicum frutescens*), Gotu Kola - Indian Pennywort (*Centella asiatica*), Cinnamon (*Cinamomum verum*), Coleus (*Coleus forskohlii*), Hawthorn (*Crataegus oxyacantha*), Ginkgo (*Ginkgo biloba*), Lavender (*Lavanula officinalis*), Ginger, Prickly ash (*Zanthoxylum americanum*), Niacin, Hawthorn berry, capsaicin, flavonoids (extractable from most plants in particular flowers, leaves and berries, for example rosemary leaves), and L-arginine, alcohol, menthol. Examples of drug substances which have topical vasodilatory effects include adenosine, glyceryl trinitrate, nitroprussides, phentolamine, histamines, prostaglandins and bradykinin. The use of capsaicin (extractable from peppers) is especially preferred.

The vasodilator may typically be present in the vasodilator composition at a concentration of 0.001 to 10% wt, especially 0.01 to 10% wt, particularly 0.1 to 2% wt.

The vasoconstrictor used according to the invention likewise may be a natural or synthetic material and may be a drug substance or a naturally occurring material, e.g. a plant extract or fragment. Most preferably it is a natural plant extract or fragment (e.g. powdered plant material). Examples of natural vasoconstrictors include Horse Chestnut, Aloe Vera, Marigold (*Calendula*

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Officinalis), German Chamomile (*Chamomilla recutita*), Conchona (*Cinchona*), Lemon (*Citrus limon*), Myrrh (*Commiphora molmol*), Meadowsweet (*Filipendula ulmaria*), Liquorice (*Glycyrrhiza*), Witch Hazel (*Hamamelidaceae*), White Peony (*Paeonia lactiflora*), Avocado (*Perea Americana*), Chinese rhubarb (*Rheum plamatum*), rosemarinic acid (extractable from Rosemary (*Romarinus officinalis*)), White Willow (*Salix alba*), Sage (*Salvia officinalis*), Comfrey (*Symphytum officinale*), Jambul (*Syzgium cumini*), Nettle (*Urtica dioica*), Bilberry-blueberry (*Vaccinium myrtillus*), Cramp Bark (*Viburnum opulus*), and Butcher's Broom. Examples of drug substances which have topical vasoconstrictory effects include phenylephrine, naphazoline, tramazoline, methoxamine, metaraminol, ephedrine, and vasopressin. The use of witch hazel is particularly preferred.

The vasoconstrictor may typically be present in the vasoconstrictor composition at a concentration of 0.01 to 10% wt, especially 0.05 to 2% wt.

The vasodilator is intended to be applied to the majority of the exposed (i.e. external) lip surface, excluding perhaps the outer periphery. It thus may take any administration form suitable for this mode of application, e.g. a stick, powder, cream, paste, ointment, solution, suspension, dispersion, impregnated fabric (e.g. a "wipe" or tissue), spray, etc. Particularly suitably it is in impregnated fabric, cream, lipstick, or liquid form, in the latter case desirably presented in a container provided with an applicator, for example a brush or absorbent pad. The composition may contain other cosmetic components, for example carriers (e.g. fabric or solvent), colorants, moisturizers, oils, waxes, pH modifiers, aromas, reflectants (e.g. light reflecting particles), fillers, etc. Particularly desirably it will contain an alpha-

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hydroxy acid (i.e. a cosmetic component known to plumpen and fill out the skin by causing moisture retention). Examples of suitable alpha hydroxy acids include glycolic acid, lactic acid, malic acid, citric acid, alpha-hydroxyethanoic acid, alpha-hydroxyoctanoic acid, and alpha-hydroxycaprylic acid, in particular glycolic and malic acids.

If desired, the vasodilator may wholly or partially be in sustained release form, e.g. dissolved or dispersed in a persistent ointment, or encapsulated in liposomes or absorbed into porous or hollow particulate carriers, for example particles of porous silica or other essentially inert materials, typically particles having a mode particle size of the order of 1 to 10 μm .

Especially desirably, all components in the vasodilator composition are naturally occurring organic or inorganic materials, especially plant components, fragments, extracts, or fermentation or digestion products. Particularly preferably the composition is free of colorants (the vasodilator itself by increasing blood flow to the lip surface will have the effect of making the lips appear more red).

If desired, physiologically tolerable strontium compounds, e.g. strontium chloride, which applied topically combat dermal irritation and subdermal pain, may be included in the vasodilator compositions.

If desired the vasodilator composition may contain mint oil or a local anaesthetic to reduce any sensation perceived by the user.

The vasoconstrictor composition likewise may take any administration form suitable for application to the periphery of the lips, e.g. sticks, pencils, liquids,

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etc. Particularly desirably it is presented in a form which allows a relatively narrow line of composition, e.g. 0.5 to 3 mm wide, to be applied. To this end the composition is preferably presented as a stick or pencil or as a liquid in a container provided with an applicator, for example a brush or absorbent pad. Again the composition may contain further optional ingredients of the type mentioned above in relation to the vasodilator composition; and again it is preferred that the composition is colorant-free and that it contains only natural components. Once again the composition may if desired contain the vasoconstrictor wholly or partly in sustained release form.

The vasodilator, where used on the lips, is preferably one having a symmetric action, or, if asymmetric one which counteracts a prevailing asymmetry in lip engorgement.

The vasoconstrictor may, if desired, be applied only to the periphery of the lips, e.g. to delineate the lips before the vasodilator is applied.

In a particularly preferred embodiment of the invention, the vasoconstrictor is applied to a surface area greater than that in which a constriction of the skin is desired, and in particular it may be applied, preferably before the vasodilator, to the region in which an engorgement of the skin is desired. Thus, the vasoconstrictor may suitably be applied as a general wash or smear over substantially the entire external lip surface (or other treated surface, e.g. as discussed below). In this way a synergy between the vasoconstrictor and vasodilator may result in an enhanced skin engorgement or blood flow enhancement in the regions where both are applied.

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Especially preferably the vasodilator is capsaicin and the vasoconstrictor is witch hazel.

The vasoconstrictor is conveniently 50:50 by volume lemon juice and distilled witch hazel solution BPC. The vasodilator is conveniently 100 mg niacin dissolved in 0.5 mL olive oil with 1 mL menthol oil (Japanese oil of peppermint) added together with 1 mL hawthorn berry extract (2 g/mL in ethanal) and 1 mL 0.0017% wt. capsaicin. This may be mixed with honey and petroleum jelly, e.g. about 1 g of each, and mixed thoroughly.

The components conventionally used in cosmetics for application to the lips and facial skin are well known in the art and do not require further discussion here.

The compositions are desirably packaged in kit form with an external container or case containing separate containers containing the two compositions and a printed form or label setting forth instructions for the application of the two compositions to the lips. In one preferred embodiment a single container or support contains both compositions, e.g. in the form of a two-ended lip pencil or combined lipstick/lip pencil.

The effect of the compositions is a lip emphasis which can last for many hours, e.g. at least 5 hours, preferably at least 8 hours.

The vasodilator composition of the invention may also, if desired, be used as a cheek blusher. This use is also deemed to form part of the present invention.

A further aspect of the invention is the use of a composition containing a vasodilator to minimize the appearance of wrinkles or fine lines on the skin's surface, optionally in conjunction with a composition

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containing a vasoconstrictor. Vasodilation will cause an increase in blood flow which would cause tissue swelling. The use of a combination of vasodilator and vasoconstrictor allows a selective increase and decrease in blood flow to defined regions and thus minimizes the appearance of wrinkles.

Thus, viewed from a further aspect the invention provides a cosmetic kit comprising: a first topical cosmetic composition comprising a physiologically tolerable vasodilator and at least one cosmetic carrier or excipient; a second topical cosmetic composition comprising a physiologically tolerable vasoconstrictor and at least one cosmetic carrier or excipient; optionally instructions for the application of said compositions to areas affected by wrinkles; and optionally a container or support for said compositions.

Viewed from a further aspect the invention also provides a topical cosmetic composition comprising a physiologically tolerable vasodilator and at least one cosmetic carrier or excipient, and instructions for the application of said composition to the surface of the skin optionally in conjunction with the application of a further topical cosmetic composition comprising a physiologically tolerable vasoconstrictor to a defined region.

Viewed from a yet further aspect the invention provides a method of cosmetic treatment to lessen the appearance of wrinkles, said method comprising applying to the surface of the skin an effective amount of a physiologically tolerable vasodilator and optionally applying to a defined region an effective amount of a physiologically tolerable vasoconstrictor.

In the above embodiments, the use of vasodilator alone

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is preferred for use on fine lines on the skin's surface, whereas the combination of vasodilator and vasoconstrictor may be preferred to minimize the appearance of deeper wrinkles. In the latter case, the vasodilator composition may be applied to, and around, the area of the wrinkles, whereas the vasoconstrictor composition may be applied to regions where blood flow is desired to be decreased e.g. around the edge of wrinkles to even out the skin's surface. The use need not be limited to wrinkles, the effect of a non-surgical "face-lift" could be achieved by applying vasoconstrictor and/or vasodilator to certain areas of the face.

The compositions of the invention are also suitable for treatment of wounds as they may promote blood flow in a manner that will optimise the likelihood that healing will occur and particularly after debridement (physical removal of dead and decaying tissue - including biofilm - from in and around the wound). Thus a further aspect of the present invention provides a formulation for the prevention of the formation of chronic wounds and ulcers (i.e. used as first signs appear or even as a preventative measure before first signs appear) or for the promotion of the healing of wounds before or after they become chronic.

This could be undertaken in any of the following ways or combinations of ways:

- a) by application directly to the potential wound site
- b) by application directly to the wound perhaps in combination with other beneficial agents such as an antimicrobial/antibio-film agent in a formulation that would maintain an optimum healing environment
- c) by application around the wound site.

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A further use for the compositions of the invention is the alleviation of the symptoms of circulatory disorders, especially Raynaud's disease. Sufferers of this condition experience pain, tingling or numbness to certain parts of the body, especially the extremities. Thus the present invention provides the use of a first topical composition comprising a physiologically tolerable vasodilator and a second topical composition comprising a physiologically tolerable vasoconstrictor in the manufacture of a medicament for the treatment of circulatory disorders, especially Raynaud's disease.

The compositions of the invention are also suitable for: combating baldness (for example by increasing blood flow to defined areas of the scalp); reducing unwanted hair growth (for example by reducing blood flow to defined areas); strengthening nails (for example by increasing blood flow to the nail bed) and the control of acne spots (for example by reducing blood flow during the day to reduce redness and/or increasing blood flow at night to speed up the cell cycle).

The invention will now be described further with reference to the following non-limiting examples.

Example 1

Lip Ointment

1% wt of Capsaicin is worked into the skin ointment commercially available under the trade name Vaseline®. Unguentum Merck may be used in place of Vaseline® and L-arginine or menthol may be used in place of capsaicin.

Example 2

Lip liner

0.12% wt witch hazel is worked into a soft wax (or petroleum jelly) which can then be applied with a brush

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or spatula.

Example 3

Formula A - Lip Ointment

Ingredients expressed as percentage weight/volume

47% Hawthorn berry extract Fresh plant tincture
Crataegus oxyacantha prepared from organically
cultivated or wild herbs in Switzerland
23.5% New Zealand Clover Honey
23.5% Vaseline
5.88% Japanese Oil of Peppermint
2.35% Niacin B3

Example 4

Formula B - Lip Ointment

Ingredients expressed as percentage weight/volume

40% Hawthorn berry extract Fresh plant tincture
Crataegus oxyacantha
2% Niacin B3
20% Japanese Oil of Peppermint
20% New Zealand Clover Honey
20% Vaseline
0.00017% Capsaicin
10% Extra virgin Olive Oil

Example 5

Lip liner

50% w/v Lemon Juice
50% w/v Witch Hazel

Example 6

Lip Enhancement Study

Selection of Study Participants

Local ethical committee approval was obtained for the study prior to commencing. 30 healthy women aged between 20-56 were recruited for the study.

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Study Method

Volunteers were randomly assigned to one of two groups. Group 1 (n=18) had formulation A applied to both lips and group 2 (n=12) had formulation B applied to both lips. Two observers carried out all of the measurements.

Baseline measurements of lip diameter (upper and lower) were taken at three points. The same three points were measured throughout the study using, reference points were marked on clear acetate sheet (the same reference points were used for each subject throughout the study). The diameter of the lips at the three marked reference points was measured using vernier callipers. Photographs of the closed lips were taken using a standard reference point (baseline photographs). The lip liner (of Example 5) was applied around the perimeter of the lips using a small applicator. Immediately afterwards, either formulation A or B was applied to the surface of the lips. No other colour-enhancers were used.

Repeated measurements and photographs of the lips were taken throughout the course of the study (up to 300 minutes post application).

Results

Formulation A

61% of subjects exhibited a defined quantitative enhancement of the lips. No quantifiable response was recorded for the other 39% of subjects.

There was an immediate statistically significant increase in diameter from baseline ($P < 0.03$) by analysis of variance with a protected least squares difference post hoc test. The positive response remained highly

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significantly increased from baseline for up to 300 minutes.

The maximum recorded response to the formulation was close to an 80% augmentation of lip size.

Photographs showed clearly defined enhanced lips of one subject, before and after application of lip liner and Formulation A.

Formulation B

This formulation resulted in a significant increase in lip diameter and definition in a large majority (83%) of subjects. Only 17% showed no quantifiable response.

There was a statistically significant increase in diameter from baseline ($P < 0.03$) by analysis of variance with a protected least squares difference post hoc test. The positive response remained highly significantly increased from baseline for up to 250 minutes.

The maximum recorded response to the formulation was above 80% augmentation of lip size, which was sustained for up to 250 minutes.

Photographs showed clearly defined enhanced lips of one subject, before and after application of lip liner and Formulation A.

Conclusions

Formulation A or B plus the lip liner resulted in significant increase in lip size and definition. Both treatments were active over a long time period. The effects were found to be fully reversible and no side-effects were reported. The formulations were well tolerated by subjects. All subjects reported a self-

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perceived increase in size and definition of the lips. This technique of lip enhancement is non-invasive, simple to apply and uses natural agents.

It is noted that formulation gave an asymmetric effect. Without wishing to be bound by theory, it is thought that this is linked to the human body's asymmetry. For example the orbicularis oris muscle is one of the muscles lying beneath the lip area. It is a concentric band of muscle that loops around. It is one part actually of the complex group of muscles for facial expression. Functional or anatomical asymmetry in the lips or underlying musculature and vasculature may affect the vasodilator mechanism.

Formula A

Proposed mechanism of action: the agents act directly on receptors on the blood vessels resulting in sub-maximal vasodilatation of arterioles and capillaries supplying the lips and surrounding musculature and support structures. The resulting slight asymmetry may well reflect the tendency to "right handedness" in the human population as a whole and accentuate any slight differences that may be present in muscle or vasculature responsiveness.

Formula B

Proposed mechanism of action vasodilatation of blood vessels in the vicinity of the lips and stimulation of vanilloid receptors in producing locally released endogenous mediators that enhance the action of the vasodilators. The result: widespread dilatation by direct and indirect mechanisms resulting in a greatly enhanced increase in blood flow to the region. Vessels are dilated to a maximal diameter, thereby minimising any differences in facial asymmetry (functional or anatomical).

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Lip liner

Vasoconstriction of the vessels surrounding the vermillion - skin border, thereby limiting the vasodilatation of the lips to the red area of the lips and not the surrounding musculature and supporting areas. Vasoconstriction around the circumferential skin-skin border would result in accentuating the vasodilatation and allow a clearer definition of the lips.

Example 7Lip Enhancement

The following tests are carried out using formulation B of Example 4.

1. Lip liner to line lips.
2. Lip liner to line lips with formulation B over the lip.
3. Lip liner to line lips and over lip followed by formulation B over lip.
4. Variations of the above but applied to one lip only.
5. Variations of the above but with each lip treated differently.

Greatest enhancement of lip volume is found using tests 2 and 3.

Example 8Wrinkle Treatment

A randomised double-blind trial is carried out involving application of a standardised quantity of either formulation (A or B) or suitable placebo to the skin of subjects with mild, moderate or severe wrinkles.

The degree of wrinkles is assessed using qualitative (self-assessment questionnaires) and quantitative

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measurements (photography, digitization, computer evaluation of wrinkles).

A noticeable reduction in the appearance of wrinkles is found following treatment with formulation A or B.

Example 9

Wound Healing

A randomised double-blind trial design is carried out involving application of standardised quantity of either formulation (A or B) or suitable placebo to skin lesions (mild, moderate and severe). The formulation is applied either directly to the wound site (alone or in combination with other beneficial agents such as an anti microbial/anti bio-film agent in a formulation that would maintain an optimum healing environment) or around the wound site. The rate and degree of wound healing is assessed using qualitative (self-assessment questionnaires) and quantitative measurements of wound healing (photography, digitization, computer evaluation of wound size, degree of scarring, blood flow).

Example 10

Raynaud's disease

Formulation B was applied to a defined area of skin on the forearm on a non Raynaud's control subject. This resulted in widespread reddening of the immediate area and vicinity of the initial area of application indicating substantial vasodilatation. The effect was long lasting (approx 3 hours).

Example 11

Raynaud's disease

A randomised double-blind trial design involving application of standardised quantity of either formulation (A or B) or suitable placebo to the skin of Raynaud's sufferers (mild, moderate and severe

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Raynaud's) is carried out. Topical application of various formulation strengths and types - dependent on the area to be treated - fingers, toes, nose, ears and more extensively for hands and feet and parts of or entire limbs for all levels of disease (mild, moderate and severe) is performed. The degree of vasodilatation is assessed using qualitative (self-assessment questionnaires) and quantitative measurements of blood flow (laser Doppler flow meter, thermal imaging, scanning of limb and evaluation of colour changes). Favourable results are found.

Claims:

1. A cosmetic kit comprising: a first topical cosmetic composition comprising a physiologically tolerable vasodilator and at least one cosmetic carrier or excipient; a second topical cosmetic composition comprising a physiologically tolerable vasoconstrictor and at least one cosmetic carrier or excipient.
2. The kit as claimed in claim 1 wherein said vasodilator is capsaicin or hawthorn.
3. The kit as claimed in claim 1 or claim 2 wherein said vasodilator is present in the vasodilator composition at a concentration of 0.01 to 10% wt.
4. The kit as claimed in any one of the preceding claims wherein said vasoconstrictor is witch hazel.
5. Use of a kit as claimed in any one of claims 1 to 4 in lip enhancement.
6. Use of a kit as claimed in any one of claims 1 to 4 to lessen the appearance of wrinkles.
7. A cosmetic kit comprising: a first topical cosmetic composition comprising a physiologically tolerable vasodilator and at least one cosmetic carrier or excipient; a second topical cosmetic composition comprising a physiologically tolerable vasoconstrictor and at least one cosmetic carrier or excipient; optionally instructions for the application of said compositions to the lips and lip periphery; and optionally a container or support for said compositions.
8. A topical cosmetic composition comprising a physiologically tolerable vasodilator and at least one

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cosmetic carrier or excipient, and instructions for the application of said composition to the surface of the lips in conjunction with the application to the periphery of the lips of a further topical cosmetic composition comprising a physiologically tolerable vasoconstrictor.

9. A topical cosmetic composition comprising a physiologically tolerable vasoconstrictor and at least one cosmetic carrier or excipient, instructions for the application of said composition to the periphery of the lips in conjunction with the application to the surface of the lips of a further topical cosmetic composition comprising a physiologically tolerable vasodilator.

10. A method of cosmetic treatment to emphasize the lips, said method comprising applying to the surface of the lips an effective amount of a physiologically tolerable vasodilator and applying to the periphery of the lips an effective amount of a physiologically tolerable vasoconstrictor.

11. The use of a topical composition comprising a physiologically tolerable vasodilator and a topical composition comprising a physiologically tolerable vasoconstrictor in the manufacture of a medicament for the treatment of circulatory disorders, especially Raynaud's disease.

12. The use of a topical composition comprising a physiologically tolerable vasodilator and a topical composition comprising a physiologically tolerable vasoconstrictor in the manufacture of a medicament for the treatment of wounds.