




SEPICONTROL™ A5

Purifying dermoprotector :
For the treatment of oily, acne prone skins

- 
- **Glycine biovector containing Cinnamon extract**
 - **Purifier of cutaneous state (tested in vivo)**
 - **Regulates sebum production**
 - **Decreases acne type lesions**
 - **5 modes of action to regulate oily, acne prone skins (5 alpha reductase, bacteria proliferation, lipase, elastase, and free radicals)**
 - **Excellent tolerance**



CONTENTS

I - OBJECTIVATION FILE

1 - Oily, acne prone skins

2 - SEPICONTROL A5: an original concept

3 - SEPICONTROL A5's *in vivo* effectiveness

3.1 – Comedo reduction

3.2 – Cutaneous lipid rate regulation

3.3 – Volunteer assessment of effectiveness

3.4 – Cutaneous regulator

4 - SEPICONTROL A5's action : 5 areas of action

4.1 – Regulation of sebum production : action on 5 α reductase

4.2 – Re-equilibrium of the cutaneous ecosystem : action against bacteria proliferation

4.3 – Inhibits the formation of free fatty acids : action against bacterial lipases

4.4 – Inhibits inflammation : action against inflammatory elastases

4.5 – Protects the skin : action against the production of free radicals

5 - Conclusion

II – TOXICOLOGICAL FILE

1 – Skin tolerance

2 – Comedogenicity

3 – Sensitisation

4 – Mutagenicity



5 - Ocular tolerance

6 - Hemolysing and denaturing power

III – TECHNICAL DATA

1 – Analytical data

2 – Regulatory data

IV - COSMETIC APPLICATIONS

V – REFERENCES



I. OBJECTIVATION FILE



1 OILY, ACNE PRONE SKINS

Many people have « oily skin », with or without acne type lesions (comedos, black heads, ...). These « small » skin problems generally break out at puberty, but they can also affect every age group. In fact, the characteristic disturbance of the sebaceous gland which provokes a more important secretion of sebum, with or without bacteria proliferation, can be aggravated by different factors such as stress, the environment, medicine or mechanical irritants (razor ...). This skin state can also simply be due to heredity.

However, it should be made clear that it is very often at puberty that these skin problems are the most difficult to live with. In fact, according to recent surveys, nearly one teenager in three has acne prone skin and considers this skin imbalance to be the height of his or her daily preoccupations. Because of the very aesthetic nature of this problem at a relatively critical period of existence, oily skin problems and « comedos » can often cause real psychological distress.

Be it in western or eastern countries these skin problems concern many people ...

*Be they due to puberty, climate, stress, pollution or simply the skin's genetic make-up, it is **important that cosmetic active ingredients can be able to help those people concerned to regain correct cutaneous equilibrium.***

HOW TO COMBAT THIS IMBALANCE?

⇒ **Because of its versatility and effectiveness**, a new cosmetic, active ingredient, **SEPICONTROL A5**, has been specifically developed by SEPPIC's laboratories to help acne prone skin **obtain a healthier appearance: reduction of the number of comedos and regulation of sebum rate** (proven *in vivo*) ;

SEPICONTROL A5's ACTION

EFFECTIVENESS :

⇒ *Improves the state of the skin :*

- Regulates sebum production
- Decreases acne type lesions
- Has an excellent tolerance



Proven In Vivo

ACTION

⇒ *Specifically combats the 5 main causes of cutaneous imbalance :*

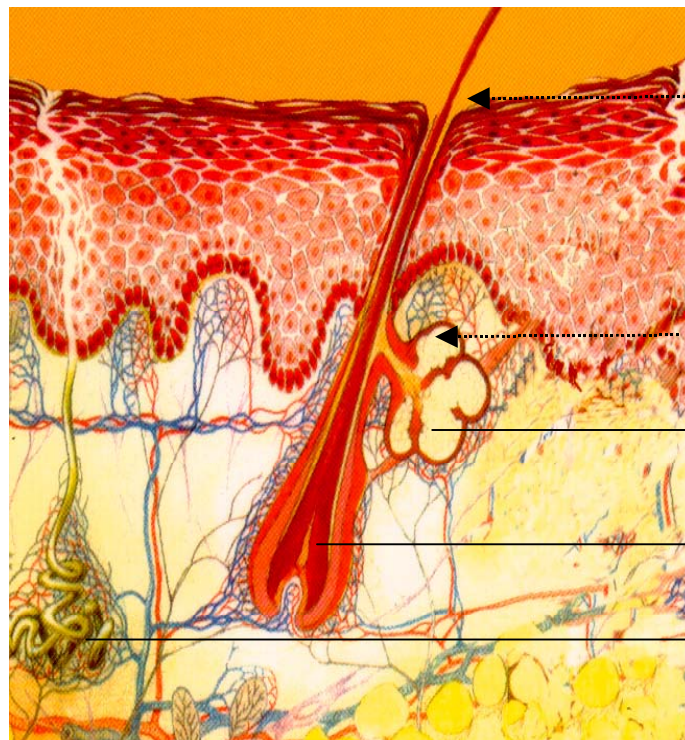
- 5 alpha reductase
- Bacteria proliferation
- Lipase
- Elastase
- Free radicals



Proven In Vitro

SEPICONTROL A5

Regulator of the skin ecosystem for oily, acne prone skins



Improves the state of the skin.

Specifically combats the 5 main causes of cutaneous imbalance.

Sebaceous gland

Hair follicle

Sweat gland

2 SEPICONTROL A5 : AN ORIGINAL CONCEPT

SEPICONTROL A5 is specially adapted to the requirements of oily, acne prone skins. Its versatility and effectiveness is obtained through the **synergistic efficacy of its different constituents (patent pending)**.

Its originality comes from three key elements :

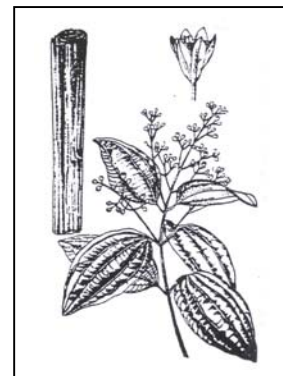
1) Selection of an essential aminoacid for the skin : glycine. In fact, glycine is the main element of dermal structure proteins (collagen, elastin...). Its presence reinforces the cutaneous barrier.

2) Bio-transformation of the aminoacid into a lipoaminoacid (grafting of glycine onto an octanoyl chain).

Naturally present in the body (e.g. : the lipoproteins contained in cell membranes), lipoamino structures are very well tolerated by the skin. Their amphiphilic structure increases their bio-affinity with skin and enables them to **vectorise the glycine** within the different layers of the epidermis. Moreover, this special structure **helps the skin restore its ecosystem**.

3) High level of cinnamon dry matter :

Originally from western India and Sri Lanka, the Cinnamon tree (part of the Lauraceae family) was introduced into many tropical countries such as the Seychelles, Madagascar, Malaysia and the West Indies. However, the plantations of Sri Lanka (those that we selected), are considered



The cinnamon bark that we use has very interesting properties for improving oily, acne prone skins :

. because of its exceptionally high catechinic tannin content, it acts as a slight **astringent**, a tonic and a **stimulant** of cutaneous cells ;

. because of its cinnamic aldehyde content, it regulates bacterial flora.



. because of its carbohydrate and mineral content (in particular, calcium oxalate,) the bark provides the nutrients required for the good health of skin cells. This need is even more important when the skin is in a delicate state.

SEPICONTROL A5 AS AN ACTIVE COSMETIC INGREDIENT:

SEPICONTROL A5 is an ideal cosmetic active ingredient because it has, in addition to its efficacy, an **excellent cutaneous bio-affinity**. Because of its **amphiphilic lipoaminoacid** structure, which is naturally present in the skin (grafting of an aminoacid onto a lipid), SEPICONTROL® A5 is not **only very well tolerated by the skin** but is also able **to go through the different layers of the epidermis more easily** to improve the state of oily, acne prone skins, more rapidly with greater effectiveness.

⇒ ***The effectiveness of SEPICONTROL A5 with oily, acne prone skins has been demonstrated in vivo on Humans.***

Its multifunctional and specific mechanism of action has been proven in vitro.

3 IN VIVO EFFECTIVENESS OF SEPICONTROL A5 WITH OILY, ACNE PRONE SKINS

The effectiveness of SEPICONTROL A5 has been demonstrated at a level of **4%** on **20 people** with oily, acne prone skin after a treatment of approximately **8 weeks** (54 days) **(1)**.

3.1 Study principle

- assessment of the **antiseborrheic effect** by analysis **of the rate of superficial skin lipids** (sebumetric measurement) ;
- assessment of its **effect on acne type lesions** (comedos) by a dermatologist ;



- assessment of the **effectiveness and the tolerance of the active ingredient** (as well as the **galenic formulation**) by the volunteers themselves.

3.2 Formula studied

SEPICONTROL A5's activity has been tested at a level of **4%** (product as sold) in a galenically acceptable formulation. The base chosen is neutral and non comedogenic.

Formula 6711 : (samples on request)

. SEPICONTROL A5	4%
. MONTANOV 202 (Arachidyl behenyl alcohols & Arachidylglucoside - SEPPIC)	3%
. DC200/50	4%
. Isohexadecane	8%
. SEPIGEL 305(polyacrylamide/C13-C14 isoparaffin / Laureth 7 -SEPPIC)	2%
. SEPICIDE HB (Phenoxyethanol/Methylparaben/ Ethylparaben / Propylparaben/ Butyl paraben - SEPPIC)	0.5%
. Fragrance	0.1%

3.3 Study protocol

The following were studied, before and after treatment :

- **Determination of the seborrheic state :**

. Measurement of the rate of superficial skin lipids using a Sebumeter™ SM 810 PC on the facial skin of 20 adult volunteers of both sexes, on the forehead, on both sides of a mid line separating the face in two. The left part of the forehead is used as a control area where no application is carried out. The right part of the forehead is the treated area, on which the product to be studied is applied.



- **Counting of acne type lesions :**

. Retentional elements (comedos ...) are counted by the dermatologist on the face of each of the volunteers.

- **Volunteer assessment of the cosmetic qualities and the effectiveness of the product applied:**

. The effect on the sebum, the shine, and the presence of spots and black heads is assessed as well as the product's special characteristics (moisturising effect, mattifying effect, texture, odour ...).

The 20 volunteers applied the product twice a day for eight weeks all over the skin of the face, with the exception of the left hand side of the forehead.

3.4 Results obtained

- **General skin appearance :**



Before treatment



***After treatment
(8 weeks)***

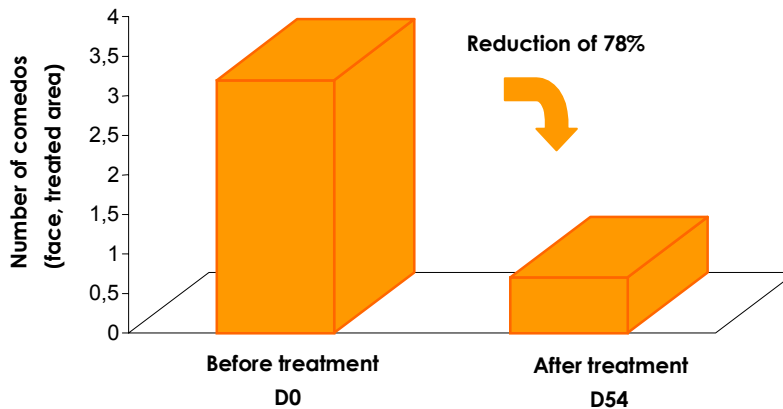
⇒ After 8 weeks of treatment, as a result of the application of **SEPICONTROL A5**, the skin becomes clearer and less oily.



- **Reduction in the number of comedos :**

A dermatologist clinically assessed the reduction in the number of comedos after 8 weeks of treatment (counting lesions on the face, before and after treatment) :

Reduction in the number of comedos after 2 months of treatment, on the area treated



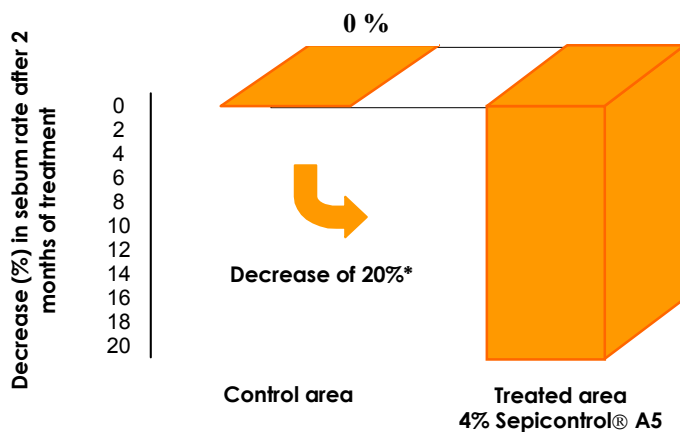
⇒ **SEPICONTROL A5 reduces effectively the number of comedos very effectively : by 78% after 8 weeks of treatment.**



- **Assessment of the cutaneous lipid rate (Sebumeter™) :**

Sebumetric measurements are carried out 30 minutes after oil removal using alcohol. This enables standardisation of the method. The superficial cutaneous lipid rate is then measured on the control area (untreated) and on the area treated before and after the eight weeks of treatment.

Decrease in the sebum rate after 2 months of treatment :



** significant decrease in comparison to the control area.*

Before treatment, the cutaneous lipid rate was identical in the two areas.

After 8 weeks of treatment, the cutaneous lipid rate is significantly reduced (by 20%) on the area treated, in comparison to the control area.

⇒ After 8 weeks of treatment, **SEPICONTROL A5 regulates sebum production (significant decrease of 20%).**

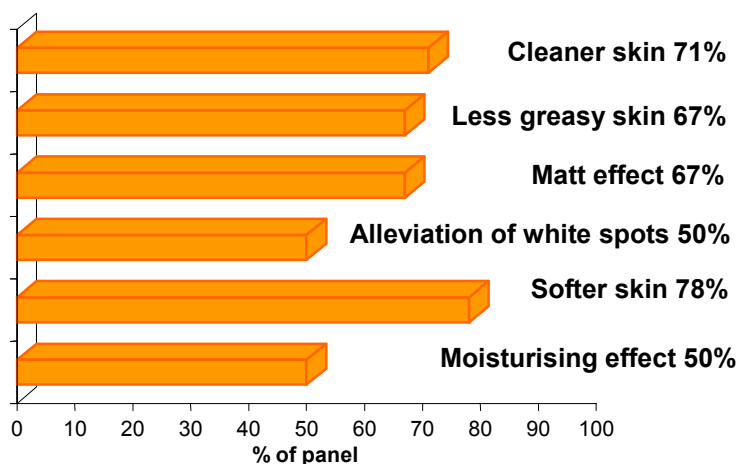
The skin then becomes less oily.



- **Sensorial assessment of the effectiveness of the product used by volunteers :**

A very positive judgement of Formula 6711 was given by the majority of volunteers after 8 weeks of use, as much for its **cosmetic qualities** (application, texture, consistency and odour) as for **its effectiveness**.

This assessment (expressed as a % of the panel) is recorded on the following graph :



The application of the **formula** studied was therefore judged to be very **pleasant and effective** according to the majority of volunteers.

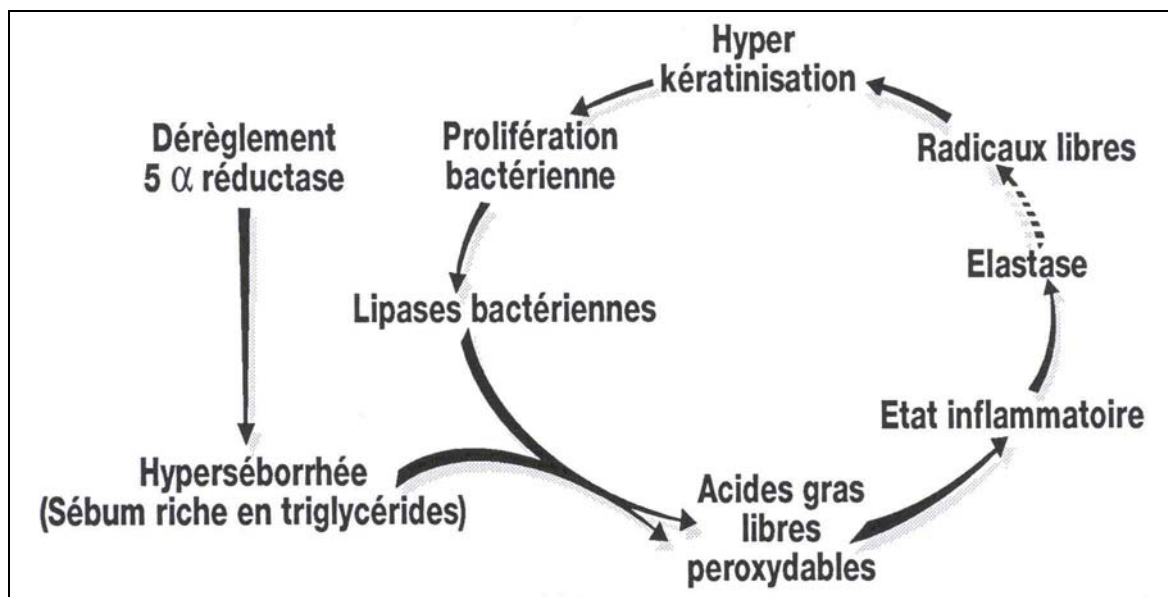
⇒ After 8 weeks of use, **the skin becomes cleaner, less oily, more matt and free of imperfections.**

When it is moisturized, the skin also becomes softer and more supple.

⇒ **Because it is very well tolerated, SEPICONTROL A5 is therefore an active ingredient which is completely suited to the requirements of oily, acne prone skin.**

4 SEPICONTROL A5'S ACTION

To understand SEPICONTROL A5's action mechanism, it is necessary to clearly define the **major causes of the imbalance occurring in oily, acne prone skins**:



This imbalanced state of skin has several causes which individually and collectively complicate its improvement.

In fact, this imbalance is firstly distinguished by a **disturbance of the 5 alpha reductase**, an enzyme present in the sebaceous glands, responsible for sebum production. This enzyme, depending on hormone levels, grows increasingly more sensitive to testosterone, its substrate. It **therefore synthesises an abnormally high rate of sebum**. It is very often during puberty, when the rate of synthesised hormone increases, that the skin becomes « oily » and « shiny ».

At the same time, **keratinisation** occurs (this is in particular due to inflammation). The skin's pores become blocked, which promotes **the multiplication of cutaneous bacteria**, especially that of *Propionibacterium acnes*, an aerotolerant bacteria. This bacteria, besides the inflammation that it causes through its



proliferation, synthesises large quantities of **lipases**. These enzymes then **break down triglycerides** present in large quantities in sebum which induces the formation of **free fatty acids** on the skin's surface.

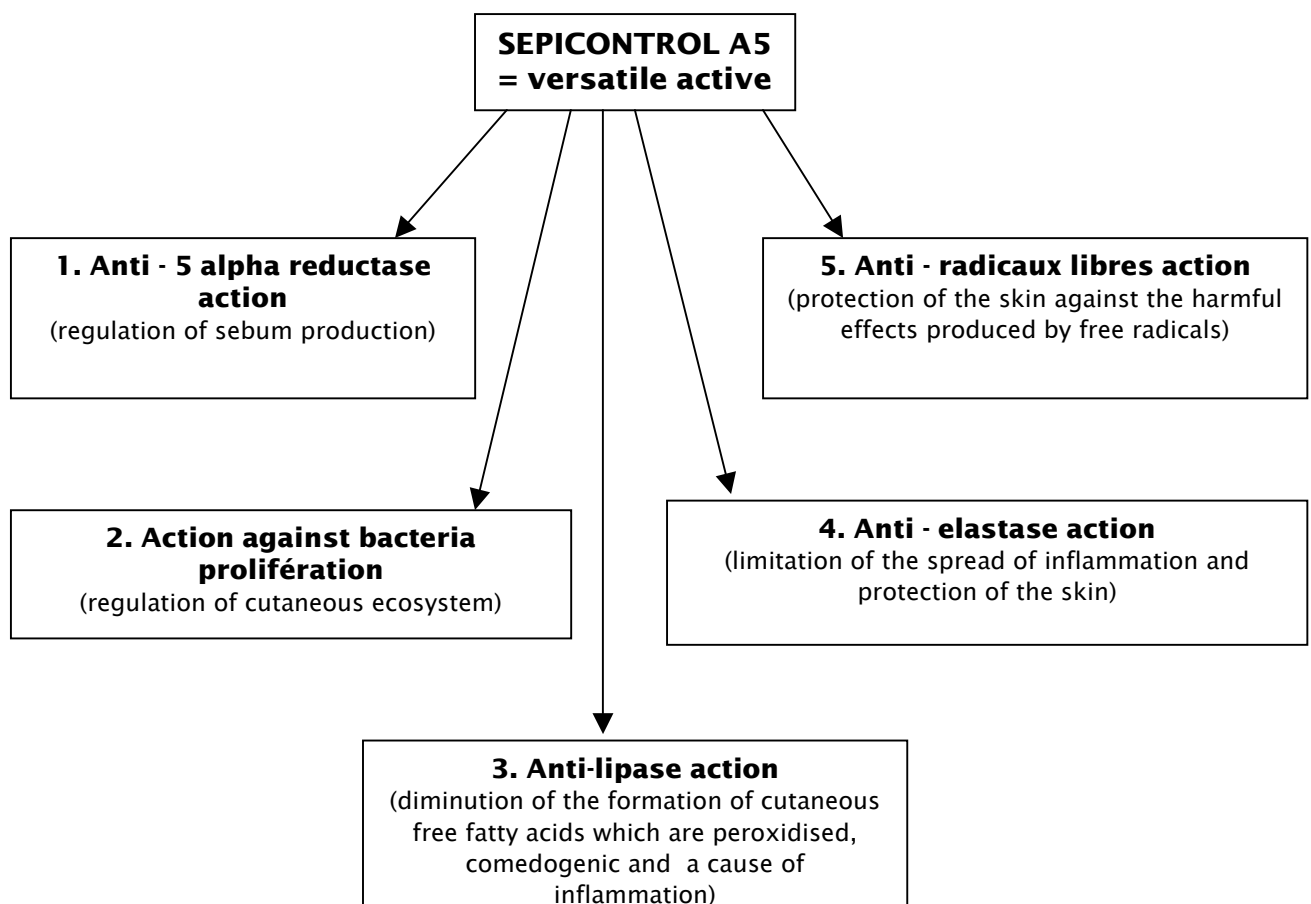
These free fatty acids are in fact the real causes of inflammation. These acids **peroxidise** very easily, as a result of the **presence of free radicals** provoked by the inflammation, they become very comedogenic. This leads to increased aggravation of the inflammation.

Different proteases, in particular **elastases**, provoked by this inflammation are going to destroy the cutaneous barrier gradually (they attack the tissue matrix : collagen, elastin..). To combat this phenomenon, the skin tries to defend itself by reinforcing epidermal synthesis, which maintains the keratinisation imbalance.

The free radicals also produced during this state of inflammation are not only going to propagate this state, but also attack all the epidermal cells, thus maximising the extent of the cutaneous disorders....

These disturbances, which are characteristic of oily, acne prone skin are therefore numerous, complex and very closely linked with each other.

In order to combat this cutaneous state effectively, **the skin must be helped by a very versatile active ingredient, able to act simultaneously against all the causes of this imbalance.**





SEPICONTROL A5's different areas of action have been demonstrated in vitro, by adapted tests.

4.1 SEPICONTROL A5's anti - 5 alpha reductase action

Hyperseborrhea or hypersecretion of sebum, is a factor constantly found in people suffering from oily skin, accompanied or not by acne type lesions.

This hypersecretion is androgen dependent and leads to an accumulation of sebum. It is in fact the sebaceous gland's increased sensitivity to hormones leads to more abundant sebum secretion.

In humans, free testosterone penetrates the sebaceous cell and is transformed into dehydrotestosterone (DHT) under the influence of the **5 alpha reductase** enzyme. The production of sebum is therefore provoked. However, this marked imbalance in oily and/or acne prone skins is not necessarily due to much higher hormone production, but rather to a hypersensitivity of 5 alpha reductase to testosterone.

For example, in some teenagers with acne prone skin, the activity of **5 alpha reductase with regards to testosterone is 2 to 20 times greater than an enzyme coming from « normal » skin.**

=> It is therefore often around puberty that this feeling of « oily skin » occurs, because suddenly the « threshold » rate of testosterone which was up until that point insufficient to induce the enzyme, is suddenly reached.

It should nevertheless be stated that androgens, which are synthesised in men in the testicles are also produced by women in the ovaries and the adrenals. This explains why this skin imbalance occurs in women as well as men.

The sebum which is accumulated in the pilosebaceous follicle obstructed by hyperkeratinisation, is then going to promote the proliferation of specific bacteria. The lipases synthesised by these bacteria, when they break down the triglycerides present in the sebum, are going to start forming free fatty acids, which are comedogenic and inflammation promoters.

=> It is therefore of the utmost importance to limit the activity of this enzyme : because of its **anti 5 alpha reductase action SEPICONTROL A5 can regulate this sebum production.**



a. Test Principle

The aim of this methods is to determine, by radiation chemistry, the extent of the 5 alpha reductase inhibition.

The 5 α -réductase transforms testosterone (marked with a carbon 14 isotope) into carbon 14 marked 5-dehydrotestosterone (5DHT).

In this experiment and in the presence of NADPH, the following reaction is measured :



5 alpha reductase is the reaction's key enzyme. Its inhibition leads both to the reduction of 5DHT as well as to the ASDs formed. The reactions are carried out in the presence and the absence of the active ingredient to be tested (control) and are chromatographically recorded on silica gel plates (dichloromethane/ethyl acetate/methanol system (85:15:3)). The 5DHT formed migrates beyond the testosterone in the system used. The ASDs formed are more polar and migrate very little.

In the presence of the active ingredient, the quantity of DHT formed is measured by autoradiography of the silica plate. This quantity of DHT formed in the presence of the active ingredient to be tested is correlated with the enzyme inhibition percentage (calculation in relation to the control reaction).

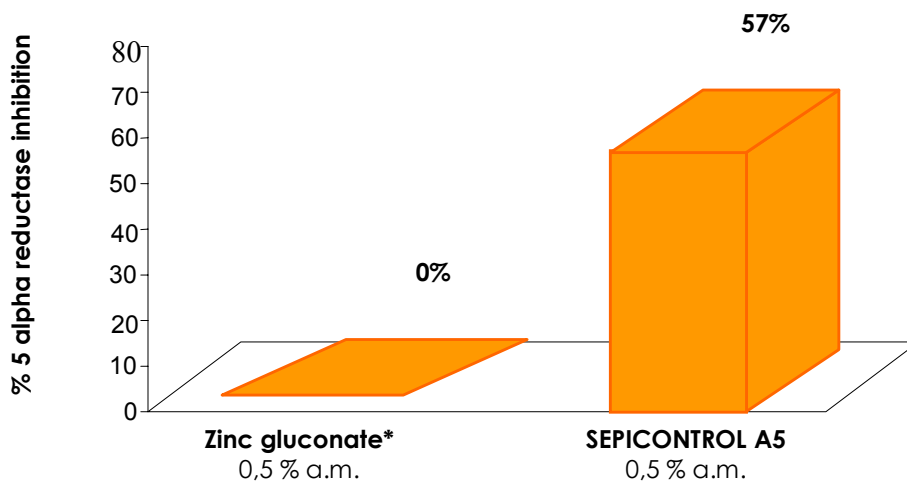
b. Results obtained

➤ First study

SEPICONTROL A5's activity with respect to 5 alpha reductase has been compared with that of a mineral currently used by the cosmetics industry to improve the state of oily skins, **zinc gluconate** (which has a known action on 5 α reductase). The products were tested at a small concentration, **0.5% (am) (2)**.



SEPICONTROL A5's anti-5 alpha reductase action compared to that of zinc gluconate :



* Zinc gluconate could be more effective against this enzyme, but at a higher concentration.

➤ **Second study**

For this study, an in vitro model of a culture of normal human dermal fibroblasts was used.

Cytotoxicity of the product was first determined so that only non-cytotoxic concentrations would be tested.

The effects of the product were compared to those obtained with finasteride, used as reference product (3).

The results confirmed, along with another model, the excellent anti-5 α reductase activity of SEPICONTROL A5.



	Control (without active ingredient)	SEPICONTROL A5 0,1% a.m.	Finasteride 30 ng/mL a.m. (positive control)
Inhibition of 5 α-reductase	0 %	40 % *	35 % *

* : statistically significant difference with the control

⇒ ***SEPICONTROL A5 effectively regulates the activity of 5 α reductase. Its action is higher than that of zinc gluconate, conventionally used to limit sebum production.***

4.2 SEPICONTROL A5's action against bacteria proliferation

Acne prone skins are distinguished by the **proliferation of specific germs in the pilosebaceous canal**. These bacteria act as inflammation promoters and are also responsible for the production of harmful enzymes to the skin.

Qualitatively, bacterial flora found on the skin and within comedos are similar in people with acne prone skin and people with a « normal » skin. Mainly staphylococci (especially, on the surface) and propionibacteria (in the pilosebaceous canal) are found.

* **Propionibacteria** are those gram-positive bacteria, formerly classified as « corynebacterium ». Propionibacteria are aerotolerant. Thus, they are mainly localised within the blocked follicle itself, where oxygen is most scarce.

Propionibacterium acnes, which is most frequently found in people with acne prone skin, produces **lipases** able to break down sebum triglycerides into free fatty acids. These free fatty acids, known for being comedogenic, are able to provoke or to maintain hyperkeratinisation of the follicle, leading to the formation of comedos.



* **Staphylococci** also colonise acne prone skins. *Staphylococcus epidermidis* and *Staphylococcus aureus*, the most frequently found, secrete elastases which are also responsible for the occurrence of acne type lesions.

Because of its action against bacteria development SEPICONTROL A5, restores normal cutaneous flora.

The effectiveness of SEPICONTROL® A5 against the germs most often associated with acne prone skins, has been compared to zinc gluconate, by determining the Minimal Inhibitory Concentration (MIC) at pH 5 (except *P. acnes* at pH7), in a liquid medium **(4) (5) (6)**.

MIC	SEPICONTROL A5 active matter (am)	Zinc gluconate active matter (am)
<i>Propionibacterium acnes</i>	0,007%	0,125%
<i>Staphylococcus epidermidis</i>	0,001%	0,5%
<i>Staphylococcus aureus</i>	0,007%	0,06%

SEPICONTROL A5's activity against germs most often associated with acne prone skins is excellent (am or as).

From the table above, if you compare active matter, SEPICONTROL® A5's efficacy is superior to that of zinc gluconate.

For the product as sold, SEPICONTROL® A5's efficacy is similar to that of zinc gluconate.

⇒ ***SEPICONTROL A5 demonstrates excellent activity against the proliferation of germs characteristically found in oily, acne prone skins.***

Its use therefore enables restoration of a normal cutaneous ecosystem, an essential factor for good balance.



4.3 SEPICONTROL A5's action against bacterial lipases

Lipase breaks down sebum triglycerides (present in large quantities on the surface of acne prone skins), into free fatty acids. By solubilising the copper or iron salts present on the skin, the free fatty acids promote lipid and protein oxidation, thus creating, locally, irritating reactions. These free fatty acids, known for being comedogenic, can cause or maintain hyperkeratinisation of the follicle, leading to the formation of comedos.

Because of its anti-lipase action, SEPICONTROL A5, reduces the formation of free fatty acids, thus limiting cutaneous irritation reactions.

SEPICONTROL A5's action with regards to lipase has been compared to that of two products currently used in dealing with acne prone skin, phenoxypropanol and zinc gluconate. These molecules are known to be lipase inhibitors. All the products have been tested at **1% (am) (7)**.

a. Test principle :

The reaction studied is the following :



A known quantity of triglycerides («Lipase Substrate/SIGMA») and a known quantity of lipase (« Control enzyme 2E/SIGMA) are put into a control test tube. After a period of incubation, the quantity of free fatty acid formed by titration with 0.05M sodium hydroxide is determined.

To test the antilipase activity of a product, it is exposed to triglycerides and lipase (Trial tube).



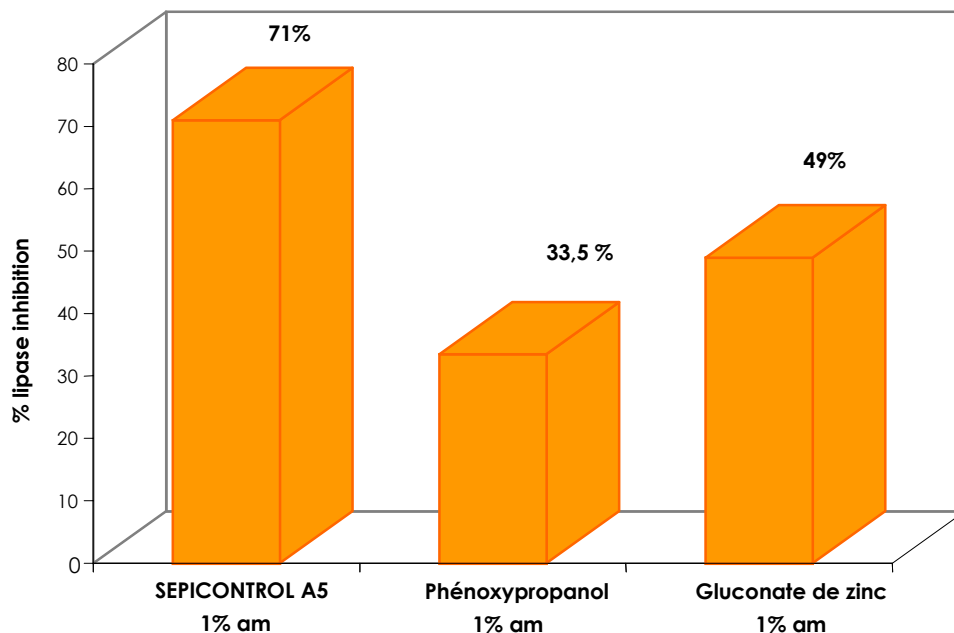
⇒ The quantity of free fatty acids formed in the presence (trial) and in the absence (control) of the substance studied is compared. Considering that the enzyme in the control tube has a 100% activity, the percentage of inhibition of the enzyme by the substance studied is deduced, using the quantity of free fatty acids formed in the « trial » tube.

For every sample tested (control or trial), it is necessary to carry out « blank » tests so as to determine the quantity of free fatty acids initially present.

Each sample must be tested twice. The result of the percentage of inhibition is therefore calculated on the average obtained.

b. Results obtained :

Anti-lipase activity of SEPICONTROL A5 compared to that of two reference products :





⇒ *Under the conditions of this test, **SEPICONTROL A5**, has an anti-lipase action which is greater than that of zinc gluconate and phenoxypropanol.*

4.4 Anti - elastase action of SEPICONTROL A5 :

Human leukocyte elastase (HLE) is presently the subject of many studies because it is involved in a large number of **inflammatory pathologies**. This enzyme, which is produced in particular when the skin is attacked, is able to **break down** many macromolecules such as fibrous **elastin**, some types of **collagen, proteoglycans** and **glycoproteins** and it is one of the links in the chain of reactions which take place during inflammation **(8) (9)**.

⇒ **Blocking this enzyme** using an anti-elastase effect therefore means stopping the break down of all these molecules and also **inhibiting the inflammation process**.

Because of its anti-lipase action, SEPICONTROL® A5 limits the spread of inflammation and stops the skin damage caused by this irritation.

SEPICONTROL A5 's anti-elastase activity has been **compared** with that of two molecules currently used in the Cosmetics industry improving acne-prone skin : **phenoxypropanol** and **zinc gluconate**. The products were tested at a quantity of **0.017% (am) (10)**.

a. Test principle :

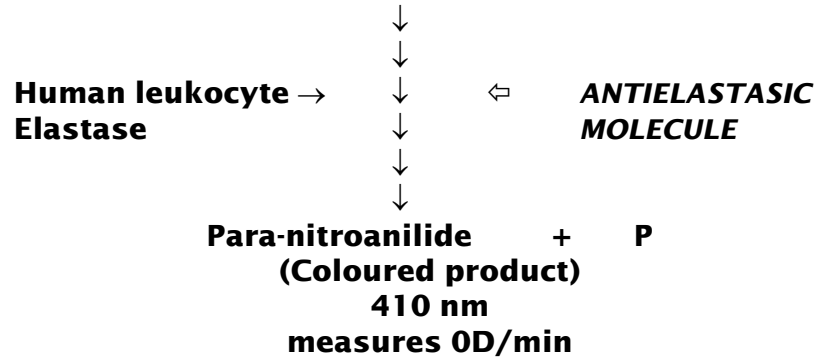
The anti-elastasic properties of a product can be demonstrated by an *in vitro* test carried out using a spectrophotometer.

These anti-elastasic properties are studied using HLE and N-methoxy succinyl - alanine - proline - valine - para-nitroanilide (colourless product). The hydrolysis of the substrate by the human leukocyte elastase liberates a coloured product, para-nitroaniline whose kinetics is monitored using a spectrophotometer at 410 nm.



The product's anti-elastasic effect is then calculated in relation to a control curve obtained without the product.

**N-methoxy succinyl - alanine - proline - valine - para-nitroanilide
(colourless substrate)**



If there is an anti-elastasic molecule

⇒ **DECREASE IN THE APPEARANCE OF THE COLOURED PRODUCT**

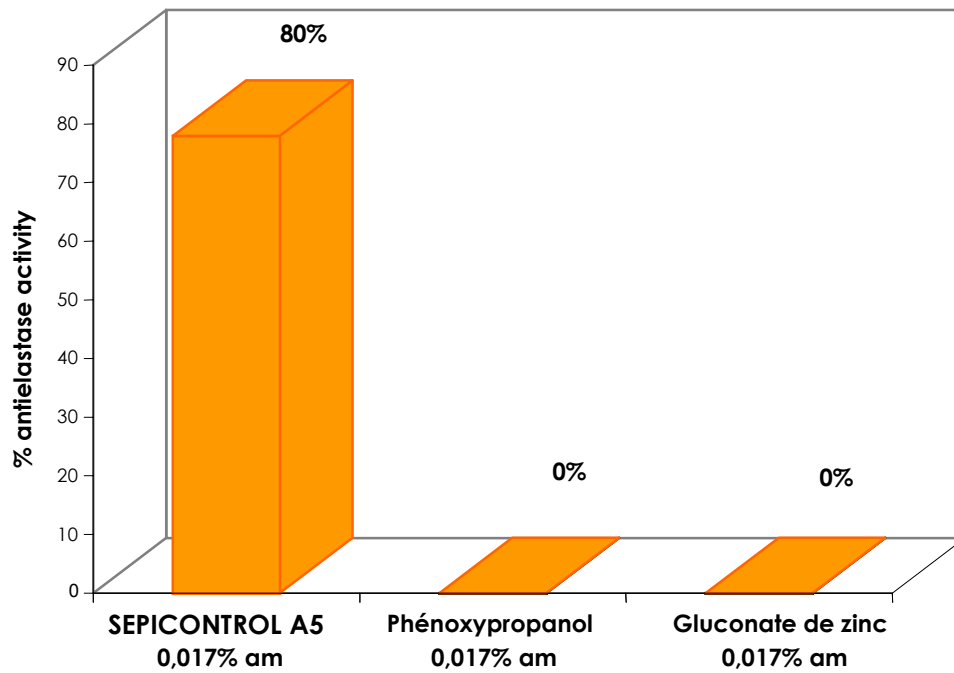
The reaction takes place in a spectrophotometer whose thermostat is set at 25°C equipped with a sample passer. All the kinetics are carried out at least three times. The average and the standard deviation are calculated for the three values obtained.

⇒ ***The percentage of inhibition of appearance of the coloured product by the active ingredient will correspond to it's percentage of HLE inhibition.***



b. Results obtained :

Anti-elastase activity of SEPICONTROL A5 compared with that of reference products used to improve the state of acne prone skins:



⇒ Under the conditions of this test, **SEPICONTROL A5 has an anti-elastase activity which is significantly superior to that of other molecules** which may be used for improving the state of oily, acne prone skins.



4.5 SEPICONTROL A5's radical scavenging action

Free radicals are active chemical species, occurring *in vivo* under normal or pathological biological conditions. However, many kinds of external aggressions (chemical, mechanical, UV, stress, pollution, excessive consumption of alcohol and tobacco,...) increase their formation, leading to very negative effects on the cell **(11)**. For acne prone skins, inflammation produces these free radicals.

Within the cell, free radicals can cause peroxidation of polyunsaturated fatty acids in the phospholipid membranes, the formation of cytotoxic peroxides, the oxidation of proteins and the denaturation of DNA. All these phenomena very often contribute to **cell death**.

Outside of the cell, the free radicals can lead to a breakdown of the main constituents of conjunctive tissue (elastin, collagen ...), which contributes, in the long term, to **general skin ageing**. They also **break down superficial free fatty acids**, which maximises inflammation ...

If the enzyme or chemical detoxification systems naturally present in the body are overwhelmed (a situation which is linked to the defence capacities of each individual), the skin requires help in defending itself in the form of radical scavenging active ingredients applied topically.

Thanks to its radical scavenging action SEPICONTROL A5, enables the skin to be protected against the harmful effects produced by free radicals.

SEPICONTROL A5's radical scavenging action has been **compared** to that of several molecules used by the Cosmetics industry for their effectiveness on acne prone skins : **phenoxypropanol** and zinc **gluconate**. The products were tested at a quantity of **0.5%** (am) **(12)**.

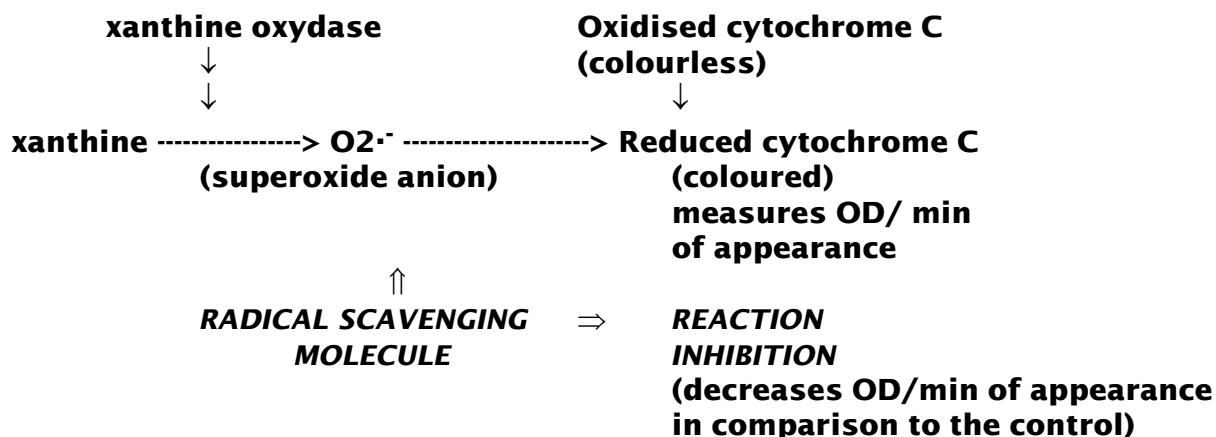


a. Test principle :

This *in vitro* test enables assessment of the radical scavenging properties of SEPICONTROL A5 with regards to the superoxide anion.

Determination of the radical scavenging effect is based on the inhibition or the decrease in the speed of reduction of cytochrome C, by adding to the reaction medium a molecule to be studied.

The superoxide anion is generated by the action of the xanthine oxydase on the xanthine. It leads, in the absence of a molecule able to capture it, to the reduction of cytochrome C. The appearance of reduced cytochrome C is observed using a spectrophotometer, set at 550 nm in the presence (Trial) or absence (Control) of radical scavenging molecules.



The reaction is carried out using a spectrophotometer whose thermostat is set at 25°C equipped with a sample passer. All the kinetics are carried out at least three times. The average and the standard deviation are calculated for the three values obtained.

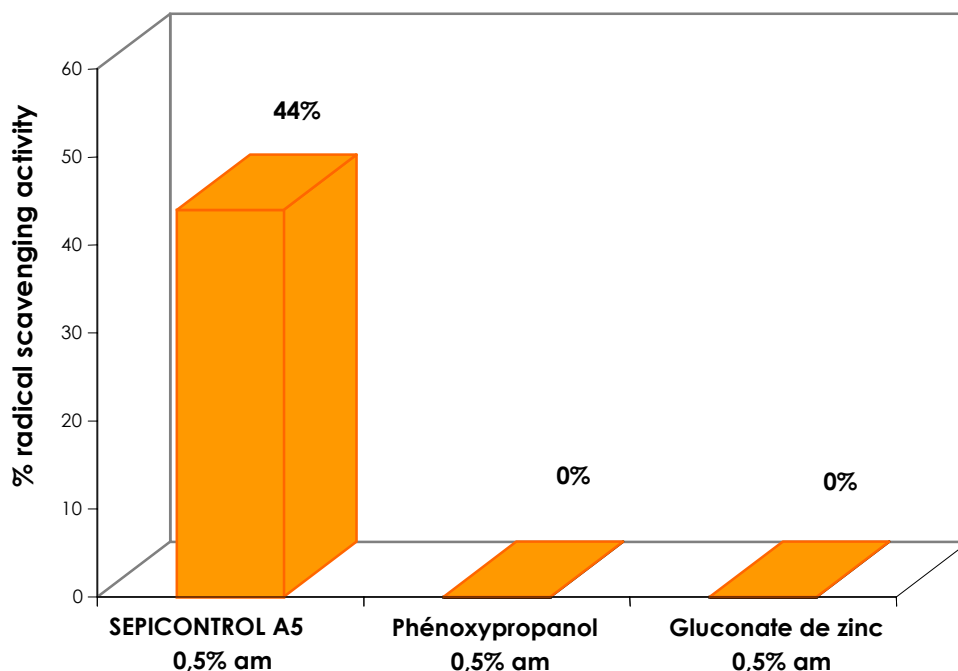
A percentage of inhibition in the speed of appearance of the coloured product (corresponding to the quantity of free superoxide anion) shall therefore be calculated for each active ingredient tested. This calculation is carried out in relation to the speed of appearance of the coloured product in the control (without active ingredient).



⇒ The percentage of inhibition in the appearance of the coloured product by the active ingredient will correspond to the percentage of inhibition of the superoxide anion (= radical scavenging activity).

b. Results obtained:

Radical scavenging activity of SEPICONTROL A5 compared to that of the reference products used to improve the state of acne prone skins:



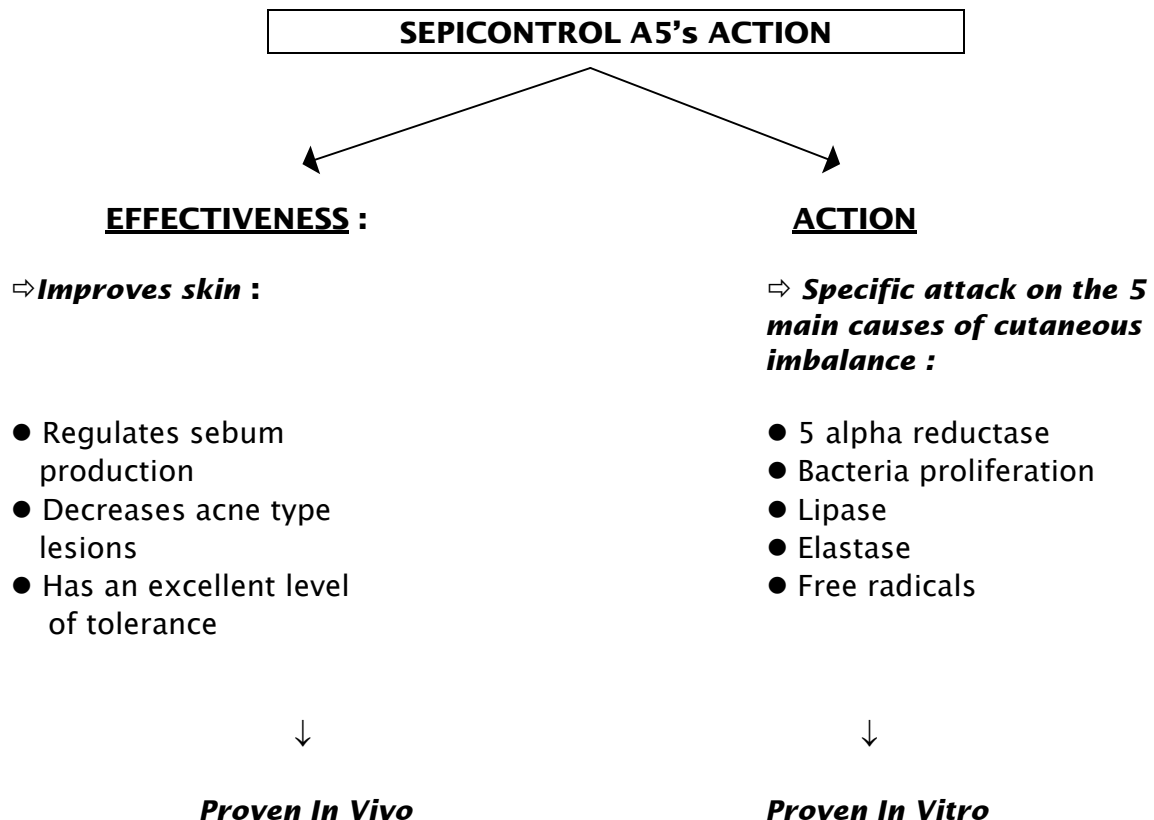
⇒ Under the conditions of this test, **SEPICONTROL A5, has a radical scavenging action which is much greater than other molecules which may be used for improving the state of acne prone skins.**



5 CONCLUSION :

Because of its 5 areas of action, proven *in vitro*, (5 alpha reductase, proliferation of specific germs, lipase, elastase and free radicals), SEPICONTROL A5 effectively regulates the state of oily, acne prone skins.

After 8 weeks of treatment, it enables a significant reduction in the number of comedos and regulates sebum production. The skin is cleaner, less oily and free of imperfections.





II. TOXICOLOGICAL FILE



1. SKIN TOLERANCE : PATCH TEST

SEPICONTROL A5 has been tested at a level of **4%** using the simple skin patch test method on **10 volunteers** (2 women and 8 men aged from 21 to 36 years old) (**13**).

Principle :

4% (a.s.) of SEPICONTROL A5 diluted in water (initial pH 5.7) was applied to the skin of the volunteers (at a rate of 0.02 ml) over a period of **48 hours** under an **occlusive patch** (Finn Chambers).

A clinical examination of the reactions caused by the product being studied was then carried out by a dermatologist, **30 minutes after the patch was removed** (clinical assessment using a scale of values).

Results :

=> No intolerance reaction was noted.

⇒ *When tested at 4% (a.s.), SEPICONTROL A5 gives a **primary skin irritation value of 0.***

SEPICONTROL A5 is therefore considered as being VERY WELL TOLERATED by the skin, at the recommended levels of use.

2. COMEDOGENICITY

When formulated at **4%** in an emulsion, SEPICONTROL® A5 was **tested dermatologically**, over **8 weeks** on **20 people** at a rate of 2 applications per day (**14**).



Emulsion 6711 :

. SEPICONTROL A5	4% (a.s.)
. MONTANOV 202 (Arachidyl behenyl alcohols & Arachidylglucoside - SEPPIC)	3%
. DC200/50	4%
. Isohexadecane	8%
. SEPIGEL 305 (polyacrylamide/C13-C14 isoparaffin / Laureth 7 -SEPPIC)	2%
.SEPICIDE HB (Phenoxyethanol/Methylparaben/ Ethylparaben / Propylparaben/ Butyl paraben - SEPPIC)	0.5%
. Fragrance	0.1%

* a.s. : product as sold

Results :

Application of the product was **well tolerated**.

⇒ ***When tested under dermatological control at 4% (a.s.) SEPICONTROL A5 is a non comedogenic active ingredient.***

3. SENSITISATION

Using the protocol of Marzulli and Maibach on 50 healthy volunteers, SEPICONTROL A5 at 2% can be considered a hypoallergenic product (15).

4. MUTAGENICITY

Using the back mutation test on strains of *Salmonella typhimurium* and *Escherichia coli* (method B14 of European Directive 92/69 and OECD Directive 471), LIPACIDE UG is considered as non mutagenic(16)



5. OCULAR TOLERANCE : HET CAM

This method is an alternative to tests on animals when assessing the ocular irritation potential of cosmetic products (17).

The principle is based on observation, by a trained person, of irritant effects (congestion, haemorrhage, coagulation) which may occur during the five minutes after the application of a product on the chorio-allantoic membrane (CAM) of a hen's egg.

This method can be used to assess the ocular irritation potential of cosmetic products (SEPPIC procedure n° 57CO 009)

Product classification :

The tested product (pure or diluted) is classified according to the scale defined in the following table :

Score (S)	Classification
$S < 1$	practically non irritant
$1 \leq S < 5$	slightly irritant
$5 \leq S < 9$	moderately irritant
$S \geq 9$	irritant

Results :

⇒ *When tested at 5% (a.s.), SEPICONTROL A5 gives a **value of 0.***

SEPICONTROL A5 is therefore considered as being NON IRRITANT, for the eyes at the recommended levels of use.



6 HEMOLYSING OR DENATURING POWER : RED BLOOD CELLS or RBCA

This method is an **alternative to tests on animals** when assessing **the irritation potential** of cosmetic products (18).

It enables assessment of the cytotoxicity of a product with regards to red blood corpuscles and a study of its denaturing power with regards to proteins (haemoglobins). (SEPPIC Procedure n° 57CO027, n° 57CO028, n° M57CO029 and n° M57CO031)

Product classification :

The product tested (pure or diluted) is classified according to the scale of values in the following table :

Score (S)	Classification
S < 10	irritant
S ≥ 10	non irritant

Results :

⇒ *When tested at 5% (a.s.) SEPICONTROL A5 is **not cytotoxic and is non denaturing.***

*SEPICONTROL A5 is therefore considered as being **NON IRRITANT at the recommended levels of use.***

⇒ **BECAUSE IT IS VERY WELL TOLERATED, SEPICONTROL® A5 IS AN ACTIVE INGREDIENT WHICH IS PERFECTLY SUITED TO THE REQUIREMENTS OF OILY, ACNE PRONE SKIN AT THE RECOMMENDED LEVELS OF USE (4% a.s.).**

* a.s. : product as sold



III. TECHNICAL DATA



1. ANALYTICAL DATA

CHARACTERISTICS	LIMITS	METHODS
Appearance	A brownish red liquid which may contain sediment	visual
pH (product as sold diluted at 3% in water)	5.6 - 6.4	European Pharmacopoeia 3 rd edition 2.2.3.
Active ingredient	35% - 40%	GL reference method currently being edited
Sulphuric ashes	7.5% - 10%	European Pharmacopoeia 3 rd edition 2.4.14
Total aerobic germs	max. 100 germs/g	European Pharmacopoeia 3 rd edition 2.6.12

Nota The values in this table are only given as indications. The only analytical specifications guaranteed are those mentioned on the certificate of analysis supplied with each delivery.

The product can solidify when cold. In this case heat the product to 60°C maximum until it becomes liquid.

Stir the product thoroughly before use to homogenise it.

Solubility :

Can be dispersed in water and in glycols.

Determination of the presence of SEPICONTROL A5 in finished products:

The presence of SEPICONTROL A5 in finished products can be identified by determining the presence of its tracer, the Capryloylglycine (using HPLC).



2. REGULATORY DATA

- INCI name:

Capryloyl Glycine (and) Sarcosine (and) Cinnamomum Zeylanicum bark extract.

- CAS and EINECS numbers :

CAS : 14246-53-8/107-97-1/84649-98-9

EINECS : 238-122-3/2035386/283-479-0

- Storage : away from heat

- Storage time : 3 years



IV. COSMETIC APPLICATIONS



Because of its **seboregulatory** and **comedolytic** properties, SEPICONTROL A5 is a new active ingredient which can be incorporated at a level of **4%** (as) into **all types of products intended for the treatment of oily or mixed, acne prone skin:**

- * **care products for oily, acne prone skin;**
- * **care products for oily or mixed skin;**
- * **hypoallergenic ranges ;**
- * **ranges for sensitive skin;**
- * **specific care products** (i.e. deodorants, hair colouring products, permanent products ...);
- * **make-up** (powder, foundation ...);
- * **milks** (make-up removing, body moisturising, after sun ...).

Because it is non-sensitising and non-comedogenic, SEPICONTROL A5 is very suitable for **hypoallergenic products**. Moreover, SEPICONTROL A5 **does not contain preservatives**.

Because it is a **liquid** and a **hydrodispersible** active ingredient, SEPICONTROL A5 can be incorporated into all types of products without any difficulty:

- * **O/W and W/O emulsions :**
 - creams, milks, wipes, foundation, ...
- * **make-up removing products**
- * **lotions and tonics**
- * **foaming and cleansing products :**
 - => shampoos, anti-dandruff shampoos, shower gels, make-up removing gels, liquid soaps, syndets, antibacterial soaps, intimate hygiene products...
 - The use of a stabilising agent (polymers ...) is recommended in this type of formula to maintain, in suspension, the tannins present in SEPICONTROL A5.

The following formulas are given as examples which illustrate the many possible applications of SEPICONTROL A5.



OILY AND ACNE PRONE SKIN CARE 6711

Formula

A	<ul style="list-style-type: none"> • MONTANOV 202 (Arachidyl behenyl alcohols & Arachidylglucoside - SEPPIC) 	3.00 %
B	<ul style="list-style-type: none"> • Water • SEPICONTROL A5 (Capryloyl Glycine (and) Sarcosine (and) Cinnamomum Zeylanicum bark extract - SEPPIC) 	qsp 100 % 4.00 %
C	<ul style="list-style-type: none"> • Dimethicone • Isohexadecane 	4.00 % 8.00 %
D	<ul style="list-style-type: none"> • SEPIGEL 305 (Polyacrylamide/C13-14 isoparaffin/Laureth-7 - SEPPIC) 	2.00 %
E	<ul style="list-style-type: none"> • SEPICIDE HB (Phenoxyethanol/Methylparaben/Ethylparaben/Propylparaben/Butyl paraben - SEPPIC) • Fragrance 	0.50 % 0.20 %

Procedure

Heat B to 85°C. Add the MONTANOV 202 (flakes) and stir until it is completely melted. Add C without previously heating it. Homogenise using the emulsifying equipment. Start to cool it very slowly. At 70°C introduce the SEPIGEL. At 60°C stop the emulsifying equipment, put the mixture under vacuum and continue cooling whilst stirring slowly. At approximately 30°C introduce the constituents of E.

Comments

SEPICONTROL A5

An active ingredient for oily, acne prone skin. It controls the five major causes of this skin unbalance (bacteria proliferation, lipases, 5 α reductase, inflammatory elastases and free radicals). The skin is clearer, less oily and free of its imperfections..

MONTANOV 202

A glucolipid emulsifier of vegetable origin which produces shiny and non oily emulsions with a soft, light and non oily feel. MONTANOV 202 has been tested and found to be non-comedogenic.

SEPIGEL 305

An emulsifying and thickening agent in a liquid, very easy-to-handle form.

SEPICIDE HB

A preservative system

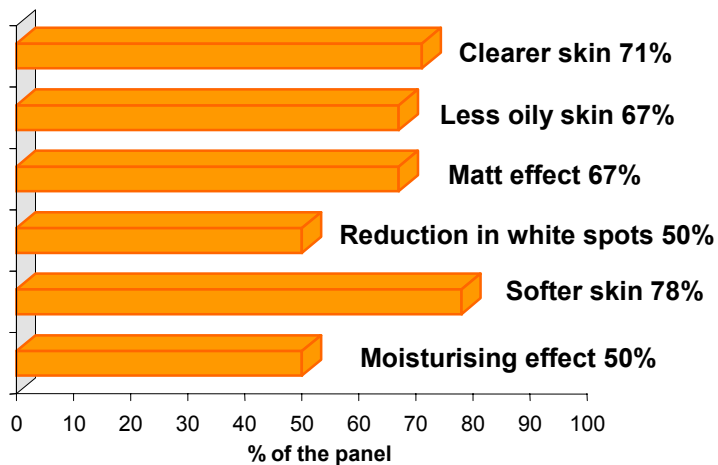


Characteristics

Appearance	Peach coloured milk
pH	Approx 5.5.
Viscosity	17 000 mPa.s BROOKFIELD LVT M4V6.
Stability	stable at RT/40/50°C stable during freeze/thaw cycles (-5°C/+40°C) stable after centrifuging at 50°C

Assessment

Sensorial assessment of the formula's effectiveness (tested on 20 volunteers over 2 months) :
(expressed as a % of the panel)



Notes

Isohexadecane (BAYER)
Dimethicone: DC200.50 (DOW CORNING)
Fragrance : PERLE 137.011 (FIRMENICH)



CARE FOR GREASY, ACNE PRONE SKINS 6712B

Formula

A	<ul style="list-style-type: none"> • SIMULGEL 600 (Acrylamide / Sodium Acryloyldimethyl Taurate Copolymer and Isohexadecane and Polysorbate 80 - SEPPIC) 3.00 % • Octyl isononanoate 5.00 % • LANOL P (Glycol palmitate - SEPPIC) 1.00 % • MICROPEARL M310 (Crosslinked polymethyl methacrylate - SEPPIC) 1.00 %
B	<ul style="list-style-type: none"> • Purified water QSP 100 % • Xanthan gum 00.20 % • SEPICONTROL A5 (Capryloyl Glycine (and) Sarcosine (and) Cinnamomum Zeylanicum bark extract - SEPPIC) 4.00 %
C	<ul style="list-style-type: none"> • SEPICIDE HB 0.30 % (Phenoxyethanol/Methylparaben/Ethylparaben/Propylparaben/B utyl paraben - SEPPIC) • SEPICIDE CI (Imidazolidinyl urea - SEPPIC) 0.20 % • Fragrance 0.10 %

Procedure

Melt LANOL P into the oil and disperse SIMULGEL in that part, then add the Micropearl. Disperse xanthan gum under mixing and introduce B into A step by step. Then add one by one the ingredients of C.

Comments

SEPICONTROL A5

An active ingredient for greasy, acne prone skin. It regulates the 5 major causes of this type of skin imbalance(bacterial proliferation, lipases, 5 α -reductase, inflammatory elastases, free radicals). The skin becomes cleaner, less greasy and free of its imperfections.

MICROPEARL M310

An absorbent, reticulated powder with a matt effect. It diminishes the shine of greasy skin.

LANOL P

Texturising agent



SIMULGEL 600

An emulsifying and gelling agent in a liquid, easy to use form.

SEPICIDE HB/CI

A preservative system.

Characteristics

Appearance	Peach coloured gel
Viscosity	Around 20,000 cps BROOKFIELD DV LV4 6rpm
pH	Around 5 = initial PH
Stabilité	Stable at RT/40/50°C Stable after centrifuging at 50°C Stable during freeze/thaw cycles -5/+40

Notes

Fragrance : NINALIX 012.822 (QUEST)
Xanthan gum: KELTROLT (KELCO)
Octyl isononanoate: PELEMOL 89 (PHOENIX)



CURATIVE & MATTIFYING CARE for greasy skin 6761A

Formula

A	<ul style="list-style-type: none"> • Water • GIVOBIO GZn (Zinc Gluconate - SEPPIC) • SEPICIDE CI (Imidazolidinyl urea - SEPPIC) • Xanthan gum • Hydroxyethylcellulose 	QSP 100% 0.50 % 0.20 % 0.50 % 0.50 %
B	<ul style="list-style-type: none"> • SEPICONTROL A5 (Capryloyl Glycine (and) Sarcosine (and) Cinnamomum Zeylanicum bark extract - SEPPIC) 	4.00 %
C	<ul style="list-style-type: none"> • Salicylic acid • Ethanol 	2.00 % 7.00 %
D	<ul style="list-style-type: none"> • Isopropyl palmitate • MICROPEARL M305 (Methylmethacrylate crosspolymer - SEPPIC) • SEPIGEL 305 (Polyacrylamide and C13-14 isoparaffin and Laureth-7 - SEPPIC) 	5.00 % 2.00 % 3.00 %
E	<ul style="list-style-type: none"> • Fragrance • SEPICIDE HB (Phenoxyethanol/Methylparaben/Ethylparaben/Propylparaben/B utylparaben - SEPPIC) • Sodium hydroxyde 	0.10 % 0.30 % QS PH=5.5

Procedure

Disperse all the constituents of A into the water whilst stirring. When the powders have been thoroughly dispersed, add the SEPICONTROL A5. Then solubilise the salicylic acid in the ethanol (C). Disperse the MICROPEARL into the oil and add the SEPIGEL 305 (D). Form the gel by mixing A and D. When the viscosity has been obtained and the gel is smooth, add C, E and then adjust the pH at the end if necessary.



Comments

SEPICONTROL A5	An active ingredient for greasy skins which regulates the 5 elements causing skin defects (proliferation of bacteria, lipases, 5 α -reductase, inflammatory elastases and free radicals). The skin becomes cleaner, less greasy and free of its defects. In this "superactive" formula, the activity is the result of a synergy between SEPICONTROL A5/Zinc gluconate/MICROPEARL M310.
MICROPEARL M310	A lipodispersable powder with excellent absorption and mattifying properties.
SEPIGEL 305	An easy to use, liquid, emulsifying and thickening agent.
SEPICIDE HB/CI	A preservative system.

Characteristics

Appearance	:	A peach coloured gel
Viscosity	:	Approximately 18,000 cps BROOKFIELD LV S4 6 rpm
pH	:	Approximately 5.5
Stability	:	Stable at room temperature, 40°C and 50°C and during freeze/thaw cycles -5/+40

Notes

Fragrance : AGNES X010033 (QUEST)
Xanthane gum: KELTROL T (KELCO)
Hydroxyethylcellulose: NATROSOL 250M (AQUALON)



FLUID AND NON GREASY SPRAYABLE CARE For oily skins 6758A

Formula

A	<ul style="list-style-type: none">• Magnesium aluminium silicate• Aqua/Water	2.00 % QSP 100 %
	<ul style="list-style-type: none">• MONTANOV L (C14-22 alcohol and C12-20 alkylglucoside - SEPPIC)	3.00 %
	<ul style="list-style-type: none">• Isononyl isononanoate	5.00 %
	<ul style="list-style-type: none">• SEPICONTROL A5 (Capryloyl Glycine (and) Sarcosine (and) Cinnamomum Zeylanicum bark extract - SEPPIC)	4.00 %
B	<ul style="list-style-type: none">• SEPICIDE HB (Phenoxyethanol/Methylparaben/Ethylparaben/Propylparaben/B utyl paraben - SEPPIC)	0.30 %
	<ul style="list-style-type: none">• SEPICIDE CI (Imidazolidinyl urea - SEPPIC)	0.20 %
	<ul style="list-style-type: none">• Parfum/Fragrance	0.20 %

Procedure

Disperse the aluminium/magnesium silicate into the cold water. Heat the aqueous phase to 70-75°C. Introduce MONTANOV L in the heated aqueous phase. When melted, add the oil then start the emulsifier. Add the SEPICONTROL A5 directly, stop the emulsifier after few minutes then start cooling the emulsion. Introduce the ingredients of phase A at around 30°C. Adjust the final pH.

Comments

MONTANOV L

An eco-emulsifier which is perfectly adapted to the production of fluid to very fluid formulae. Its use in a formulations facilitates their stabilisation even in the presence of active ingredients which have a high electrolyte content.

SEPICONTROL A5

An active ingredient for greasy skin which regulates the 5 elements responsible for skin defects (bacterial proliferation, lipases, 5 α -reductase, inflammation, elastases and free radicals). The skin becomes cleaner, less greasy and free of its defects.



Characteristics

Appearance	A fluid, peach coloured emulsion
Viscosity	Approximately 500 cps BROOKFIELD LV2 6rpm
pH	Approximately 5
Stability	Stable at room temperature - 40°C & 50°C and after freeze-thaw cycles -5/+40°C
Assessment	3460mm ² (method 57CO035)

Notes

Fragrance : AGNES X010033 (QUEST)

Magnesium aluminium silicate: VEEGUM HS (VANDERBILT)



CARE GEL for greasy skins treating and mattifying effect 6734

Formula

A	<ul style="list-style-type: none"> • Water • Xanthan gum 	70.00 % 0.30 %
B	<ul style="list-style-type: none"> • SEPICONTROL A5 (Capryloyl Glycine (and) Sarcosine (and) Cinnamomum Zeylanicum bark extract - SEPPIC) 	4.00 %
C	<ul style="list-style-type: none"> • Isononyl isononanoate • SEPICALM VG (Sodium palmitoyl proline and Water lily (Nymphaea alba) Extract - SEPPIC) • MICROPEARL M310 (Polymethylmethacrylate - SEPPIC) 	4.00 % 1.00 % 2.00 %
D	<ul style="list-style-type: none"> • SIMULGEL EG (Sodium acrylate/acryloyldimethyltaurate copolymer and isohexadecane and polysorbate 80 - SEPPIC) 	3.50 %
E	<ul style="list-style-type: none"> • SEPICIDE HB (Phenoxyethanol/Methylparaben/Ethylparaben/Propylparaben/Butylparaben - SEPPIC) • SEPICIDE CI (Imidazolidinyl urea - SEPPIC) • Fragrance • Water 	0.30 % 0.20 % 0.20 % QSP 100%

Procedure

Disperse the xanthan gum into the water using defloculating equipment. Then add the SEPICONTROL A5. Prepare phase C separately then disperse the SIMULGEL EG into this phase. Then add [C+D] into [A+B]. Thoroughly homogenise this mixture until a smooth gel is obtained then add the ingredients of E. At the end of the procedure adjust the water content and the pH if necessary.

Comments

MICROPEARL M310 A lipodispersible powder with excellent absorbent properties and matt action on the skin.

SEPICONTROL A5 An active ingredient for greasy skins which regulates the 5 elements which cause skin defects (proliferation of bacteria, lipases, 5 α -reductase, inflammation, elastases and free radicals). The skin becomes cleaner, less greasy and free of imperfections.



SEPICALM VG

A lipoaminated, soothing, active ingredient rich in Lily Flower extract which is specially adapted to meet the requirements of sensitive skins. It helps resist external aggressions.

SIMULGEL EG

An emulsifying, thickening agent which comes in a liquid, easy to use, form.

SEPICIDE HB/CI

A preservative system.

Characteristics

Appearance	A peach coloured opaque gel.
pH	Approximately 5.7
Viscosity	Approximately 30,000 mPa.s BROOKFIELD LV S4 - 6 r.p.m.
Stability	Excellent at room temperature, 40°C and 50°C stable during freeze/thaw cycles (-10°C/+40°C / 1 month) stable after centrifuging (3000rpm - 50°C - 20')

Notes

Fragrance : NINA X018.434 (QUEST)
Xanthan gum: KELTROL T (KELCO)



CARE CREAM FOR GREASY SKIN 6713

Formula

A	• SIMULSOL 165 (Glyceryl stearate/PEG100 stearate - SEPPIC)	8.00 %
	• MONTANOV 202 (Arachidyl alcohol/behenyl alcohols & Arachidylglucoside - SEPPIC)	1.00 %
	• Caprylic capric triglycerides	5.00 %
B	• Water	QSP 100 %
	• SEPICONTROL A5 (Capryloyl Glycine (and) Sarcosine (and) Cinnamomum Zeylanicum bark extract - SEPPIC)	4.00 %
C	• SEPIGEL 305 (Polyacrylamide/C13-14 isoparaffin/Laureth-7 - SEPPIC)	2.50 %
	• Isohexadecane	5.00 %
D	• SEPICIDE HB (Phenoxyethanol/Methylparaben/Ethylparaben/Propylparaben/Butyl paraben - SEPPIC)	0.30 %
	• SEPICIDE CI (Imidazolidinyl urea - SEPPIC)	0.20 %
	• Fragrance	0.10 %

Procedure

Heat A to approximately 80°C. Heat the aqueous phase to approximately 80°C, emulsify A into B. Then add C at about 70°C. Around 30°C introduce the preservatives and the fragrance.

Comments

SEPICONTROL A5 An active ingredient for greasy, acne prone skin. It regulates the 5 major causes of this type of skin imbalance (bacterial proliferation, lipases, 5 α -reductase, inflammatory elastases, free radicals). The skin becomes cleaner, less greasy and free of its imperfections.

MONTANOV 202 A glucolipid, emulsifier of vegetable origin. MONTANOV 202 can be used as a coemulsifier of SIMULSOL 165. It significantly improves the emulsion's appearance and improves softness without any greasy effect.



SEPIGEL 305

An emulsifying and thickening agent in a liquid, very easy-to-handle form.

SEPICIDE HB/CI

Preservative system.

Characteristics

Appearance	Peach coloured cream
pH	Approximately 5.5.
Viscosity	Approximately 25,000 mPa.s BROOKFIELD LV4 6rpm
Stability	stable at RT/40/50°C stable during freeze/thaw cycles (-5°C/+40°C) stable after centrifuging at 50°C

Notes

Isohexadecane (BAYER)
Fragrance : NINALIX 012.822 (QUEST)



V. REFERENCES

- (1) IEC, Report n°70613RDE
- (2) BIOALTERNATIVE, Report n°AD970403-1D/BIS (french)
- (3) BIOPREDIC, Report n°4633-1
- (4) MIDAC, Report n°97 257 D-2
- (5) KEYBIO, Report n°B97-0957C (french)
- (6) MIDAC, Report n° 98029D-2
- (7) Antilipase activity of SEPICONTROL A5 / Internal report- SEPPIC
- (8) R. Voegeli et al, « **Elastase and tryptase determination on human skin surface** », *Cosmetic & Toiletries* ® magazine; vol 111 ; p. 51 (July 1996)
- (9) V. Bizot -Foulon et al, « **Inhibition of human neutrophil elastase by wheat ceramides** », *International Journal of cosmetic Science*, vol 17, p. 255 (1995).
- (10) Anti-elastase activity of SEPICONTROL A5 / Internal report- SEPPIC
- (11) *La Recherche* 228 ; vol 22 ; p. 56 (Janvier 1991)
- (12) Radical scavenging activity of SEPICONTROL A5 / Internal report- SEPPIC
- (13) IEC, Report n° 703991RD / Essai CS972301.
- (14) IEC, Report n° 70613RDE
- (15) EVIC CEBA, Report n° If 037/990231
- (16) SAFEPHARM, Report n°1190/009
- (17) SEPPICTOXHETCAM, Report n°1841 a
- (18) SEPPICRBCA, Report n°534 a



Note

The analytical specifications warranted are only those mentioned on the analysis certificate supplied with each delivery of the product.

Except as set forth above, SEPPIC* makes no warranties, whether express, implied or statutory, as to the product which is the subject of this document. Without limiting the generality of the foregoing, SEPPIC* makes no warranty of merchantability of the product or of the fitness of the product for any particular purpose. The buyer assumes all risk and liability resulting from the use or sale of the product, whether singly or in combination with other goods. The information set forth herein is furnished free of charge and is based on technical data that SEPPIC* believes to be reliable. It is intended for use by persons having technical skill and at their own discretion and risk. Since conditions of use are outside SEPPIC*'s control, SEPPIC* makes no warranties, express or implied, and assumes no liability in connection with any use of this information. Nothing herein is to be taken as a license to operate under or a recommendation to infringe any patents.

SEPICONTROL™5 : A registered trade mark of SEPPIC.

* SEPPIC being and, depending on the country :

SEPPIC S.A.

75, quai d'Orsay
75321 Paris cedex 07
FRANCE
Tel.: +33 (0) 1 40 62 55 55
Fax: +33 (0) 1 40 62 52 53

SEPPIC UK Ltd

50 Salisbury Road
PO Box 338 - Hounslow
TW4 6SH - ENGLAND
Tel.: +44 208 577 8800
Fax: +44 208 570 2106

SEPPIC ITALIA Srl

Via Quarenghi 27
20151 Milan
ITALY
Tel.: +39 02 38009110
Fax: +39 02 38009140

SEPPIC Inc.

30, Two Bridges Road, suite 210
Fairfield, New Jersey 07004-1530
USA
Tel : +1 973 882 5597
Fax : +1 973 882 5178

SEPPIC Shanghai

Room 303 Li Hua Fu Xing
Commercial Building
139 Rui Jin Yi Road
Shanghai 200020, China
Tel : +86-(21) 53 06 30 16
Fax : +86-(21) 53 06 86 81

Subsidiary of the AIR LIQUIDE group

www.SEPPIC.com

C/1772/GB/01/August 2001