COMMONWEALTH of AUSTRALIA
Patents Act 1952

APPLICATION FOR A STANDARD PATENT

631441

I/We

Crinos Industria Farmacobiologica S.p.A.

of

Piazza XX Settembre, 2, 22079 Villa Guardia (Como), Italy

hereby apply for the grant of a Standard Patent for an invention entitled:

Preparations for topical use containing depolymerized deoxyribonucleic acids to reduce unsightly defects of the epidermis of the face and some skin areas of the body

which is described in the accompanying complete specification.

Details of basic application(s):-

Number	Convention Country	Date
21650A/89	Italy	7 September 1989

The address for service is care of DAVIES & COLLISON, Patent Attorneys, of 1 Little Collins Street, Melbourne, in the State of Victoria, Commonwealth of Australia.

DATED this TWENTIETH day of JULY 1990

To: THE COMMISSIONER OF PATENTS

.....
a member of the firm of
DAVIES & COLLISON for
and on behalf of the
applicant(s)

Davies & Collison, Melbourne

COMMONWEALTH OF AUSTRALIA

PATENTS ACT 1952

DECLARATION IN SUPPORT OF CONVENTION OR NON-CONVENTION APPLICATION FOR A PATENT

In support of the Application made for a patent for an invention

Insert title of invention

entitled: Preparations for topical use containing depolymerized deoxyribonucleic acids to reduce unsightly defects of the epidermis of the face and some skin areas of the body

Insert full name(s) and address(es) of declarant(s) being the applicant(s) or person(s) authorized to sign on behalf of an applicant company.

I Teresio Roberto Bertani
We of Crinos Industria Farmacobiologica S.p.A.
of Piazza XX Settembre 2
22079 Villa Guardia Como-ITALY

do solemnly and sincerely declare as follows :-

Cross out whichever of paragraphs 1(a) or 1(b) does not apply

1(a) relates to application made by individual(s)
1(b) relates to application made by company; insert name of applicant company.

1. (a) I am / We are the applicant for the patent

or (b) I am authorized by Crinos Industria Farmacobiologica S.p.A.

the applicant for the patent to make this declaration on its behalf.

Cross out whichever of paragraphs 2(a) or 2(b) does not apply

2(a) relates to application made by inventor(s)
2(b) relates to application made by company(s) or person(s) who are not inventor(s); insert full name(s) and address(es) of inventors)

2. (a) I am / We are the actual inventor of the invention

or (b)

Giovanni Gazzani, via Volta 28/B - Appiano Gentile (COMO)
ITALY

is / are the actual inventor of the invention and the facts upon which the applicant

is / are entitled to make the application are as follows :-

State manner in which applicant(s) derive title from inventor(s)

Giovanni Gazzani is an employee of the firm Crinos Industria Farmacobiologica S.p.A. whereby the applicant would if a patent were granted on an application made by the said inventor, be entitled to have the patent assigned to it.

Cross out paragraphs 3 and 4 for non-convention applications. For convention applications, insert basic country(s) followed by date(s) and basic applicant(s).

3. The basic application as defined by Section 141 of the Act was made

in ITALY on the 7th day of September 1989

by Crinos Industria Farmacobiologica S.p.A.

in ..... on the .....

by .....

in ..... on the .....

by .....

4 The basic application referred to in paragraph 3 of this Declaration was the first application made in a Convention country in respect of the invention the subject of the application.

Insert place and date of signature.

Declared at Villa Guardia this 4th day of May 1990

Signature of declarant(s) (no attestation required)

Crinos
Industria Farmacobiologica spa
Dott. Teresio Roberto Bertani
DIRETTORE GENERALE

Teresio Roberto Bertani

Note Initial all alterations

(12) PATENT ABRIDGMENT (11) Document No. AU-B-59169/90
(19) AUSTRALIAN PATENT OFFICE (10) Acceptance No. 631441

(54) Title
PREPARATIONS FOR TOPICAL USE CONTAINING DEPOLYMERIZED DEOXYRIBONUCLEIC ACIDS TO REDUCE UNSIGHTLY DEFECTS OF THE EPIDERMIS OF THE FACE AND SOME SKIN AREAS OF THE BODY

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(57) Claim

1. A method of reducing the unsightly defects of the epidermis of the face caused by " couperose " as herein before defined and/or to locally reduce, on the skin of the legs and ankles the defects which appear collaterally to a prolongued fatigue of lower limbs in an animal in need thereof, comprising the step of administering topically to said animal an effective amount of depolymerized deoxyribonucleic acids having the following analytical properties, expressed as percentage in weight of the dry product :

Phosphorous	8,0	-	9,6
Nitrogen	13,0	-	15,0
Desoxyribose	17,0	-	24,0
Adenine	8,0	-	11,0
Guanine	7,0	-	9,5
Cytosine	5,5	-	7,5
Thymine	8,0	-	11,0
Adenina + Guanina / Thymine + Cytosine	0,87	-	1,01
Molecular Weight (dalton units)	10.000	-	100.000

together with one or more cosmetically suitable vehicles and/or excipients.

COMMONWEALTH OF AUSTRALIA

PATENTS ACT 1952

COMPLETE SPECIFICATION

631441

NAME & ADDRESS OF APPLICANT:

Crinos Industria Farmacobiologica S.p.A.
Piazza XX Settembre, 2
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Italy

NAME(S) OF INVENTOR(S):

Giovanni GAZZANI

ADDRESS FOR SERVICE:

DAVIES & COLLISON
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COMPLETE SPECIFICATION FOR THE INVENTION ENTITLED:

Preparations for topical use containing depolymerized deoxyribonucleic acids to reduce unsightly defects of the epidermis of the face and some skin areas of the body

The following statement is a full description of this invention, including the best method of performing it known to me/us:-

DESCRIPTION

This invention has as its first object the topical use of formulations containing depolymerized deoxyribonucleic acids to reduce unsightly defects of the epidermis of the face caused by "couperose".

A further object of the invention relates to the topical use of said formulations to reduce the unsightly defects which occur in some areas of the skin in the lower limbs attributable to a situation of prolonged fatigue of the limb, as for example may occur in subjects who in carrying out their respective activities have to stand for long periods of time.

In cases of this type, abnormally dilated capillaries, associated with oedemas, tumefactions etc., may appear locally on the skin of the legs and ankles.

In other cutaneous areas, the epidermis of the limb may instead appear livid and discoloured.

In these conditions, in the area of the limb affected by the abovementioned phenomena, there may also be a sensation of aching and/or heaviness. The active ingredients of the formulations in question, that is to say deoxyribonucleic acids of low molecular weight, are prepared by known depolymerization procedures. More particularly, said active ingredients are preferably obtained on the basis of the technique which forms the object of the USA patent no. 3.899.481.

The relative chemical and chemico-physical properties of the depolymerized deoxyribonucleic acids which are obtained according to this procedure are given in Table I. The analytical methods used to determine the relevant parameters have already been referred to in the previous European patent application no. 88.115.824, regarding the cosmetic use of the aforementioned substances as tricogen factors, to which therefore reference is made.

Prior to relating the experiments which have demonstrated the efficacy of the formulations containing depolymerized deoxyribonucleic acids in the uses provided for by this invention, it must be explained here what is meant by the term "couperose", since in the literature of the field it has been used in different ways according to the presence and contextual prominence on the skin of certain features with which it may appear.

Dermatological tests define this skin affection more correctly as telangiectasia erythrosis, since "couperose" gives rise to a reddening, widespread to a greater or lesser extent, of the epidermis of the face, in which dilated surface blood vessels are prominent (telangiectasis).

It must be pointed out here that the aforementioned reddening may be widespread over the whole face, or localised in certain zones, such as on the cheekbones, nose or under the eyes. The aforementioned telangiectasis, which accompanies, as we have seen, the reddening of the face, may at times take on characteristic shapes known as, according to the cases, "star", "stripe", "plume".

As regards the experiments which proved the feasibility of the topical use of the aforementioned formulations to reduce "couperose" and the defects of the cutaneous areas of the lower limbs, it should be noted that the main common cause of said phenomena is clearly to be found in a modification of the normal conditions of the surface vessels, more particularly regarding their mechanical resistance characteristics.

In this respect mention should be made first of all of an experiment on animals (rats), in which blood capillary resistance was lowered by administering a special diet, but nevertheless, following repeated topical applications of formulations containing depolymerized nucleic acids, demonstrated at the end of treatment a considerable increase in the capillary resistance values compared to the original state. The trial was performed on 55 animals, divided into 6 groups as shown in Table II and then treated with the formulations given in Table III. Table IV illustrates the analytical properties of the deoxyribonucleic acids which go to make up the compositions described in the aforementioned Table III.

It should be noted that in all cases the aforementioned formulations contained, as active ingredient, an equal-weight mixture of the batches given in Table IV.

5 of the 6 aforementioned groups were fed with a diet lacking in vitamin P (Charlier diet, commercially

available), which in time gives rise to a consistent reduction in the mechanical resistance of the blood vessels (G. Rialdi: "Determinazione della resistenza capillare durante trattamento percutaneo con sostanze cheratoplastiche dotate di attivita' anticouperosica" Riv. It. EPPOS 60 422-425 1978).

Capillary resistance was determined on each occasion according to the Lavollay technique (J. Lavollay et al. "Problems posed by activity of certain flavonoids on vascular resistance" in "Pharmacology of plant phenolics", Symposium Oxford, 1958, Proceedings pages 103-122, 1959).

In order to perform the required determination on the basis of the technique in question, the skin of the dorsolumbar region was shaved thoroughly and slightly smeared with vaseline oil. The zone suitable for determination was an area of circa 2 x 1.5 cm, extending in length from the last ribs and bordering in width the paravertebral fasciae.

The animals were slightly anaesthetised and then, on the dorsal region mentioned previously, the instrument for measuring capillary resistance was applied, consisting of a suction cap attached to a vacuum pump (petecchiometer, Baldinelli, Milan).

The apparatus therefore enables the value of the depression, expressed in mm Hg, capable of causing breakage of the blood vessels, to be determined.

Said determination was performed on all the groups of animals, fed with the Charlier diet, on the 21st day from the start of the experiment. It was ascertained that in all the groups the animals presented a statistically significant reduction in capillary resistance compared to the control group, which had instead been fed with a normal diet (MIL Morini diet).

Said reduction was moreover statistically significant in the various groups. The absolute value of capillary resistance of the treated animals was between 163.3 (Group B) and 183.0 (Group F); in the untreated animals (control group) it was 319.6 mm Hg.

Topical treatment was begun on the 22nd day and continued for 7 consecutive days. The cutaneous zone of the animal, on which the formulations in Table III were applied, was the same on which determination of capillary resistance according to the Lavollay technique had previously been performed.

The administrations were repeated three times a day applying topically 0.2 ml at a time of each of the aforementioned formulations or 0.2 ml of physiological solution (control group).

At the end of the treatment period the capillary resistance was again measured using the same technique. The results are given in Table V.

As can be seen therefore, topical application of depolymerized deoxyribonucleic acids by means of the formulations given in Table III and operating according to the experimental design illustrated above, all the doses

tested gave rise to a statistically significant increase in capillary resistance. Table IV moreover shows that the preparation containing 5% concentration of depolymerized deoxyribonucleic acids (group E) caused, in the treated rats, an increase in capillary resistance to a value relatively close to that of the control group. Also worthy of note is the fact that the commercial preparation containing O-(β-hydroxyethyl)-rutosidea as active principle, proved more or less as effective as the gel containing the depolymerized nucleic acids at 1.25% concentration.

TABLE I

Analytical chemical and chemico-physical parameters of the depolymerized deoxyribonucleic acids which can be used for the objects provided for by this invention.

- Phosphorous	(+)	8.0 - 9.6
- Nitrogen	(+)	13.0 - 15.0
- Deoxyribose	(+)	17.0 - 24.0
- Adenine	(+)	8.0 - 11.0
- Guanine	(+)	7.0 - 9.5
- Cytosine	(+)	5.5 - 7.5
- Tymine	(+)	8.0 - 11.0
$\frac{A + G}{T + C}$		0.87 - 1.01
- Molecular weight		10,000 - 100,000
Preferably		15,000 - 60,000

(+) these data refer to the corresponding percentages in weight of the dry product.

TABLE II

Capillary fragility induced in animals by administration of the Charlier diet. Groups, number of animals per group and relative treatment.

Group	No. of animals	Treatment
A	10	normal diet, topical treatment with physiological solution (control group).
B	10	Charlier diet, topical treatment with placebo formulation (Table III).
C	10	Charlier diet, topical treatment with gel at 1.25% concentration (Table III).
D	10	Charlier diet, topical treatment with gel at 2.5% concentration (Table III).
E	10	Charlier diet, topical treatment with gel at 5% concentration (Table III).
F	5	Charlier diet, topical treatment with a commercial preparation containing : 2 g O-(β-hydroxyethyl)-rutosides, 600 mg polymerized acrylic acid, 50 mg disodium ethylenediaminetetraacetic acid, 5 mg benzalkonium chloride, bidistilled water q.s. to 100 g.

TABLE III

Composition of the cosmetic formulations used in experiments of capillary fragility.

Components per 100g of gel	Placebo	1.25%	2.5%	5.0%
depolymerized deoxyribonucleic acids g	--	1.25	2.5	5.0
Carbopol 940 g	2.0	2.0	2.0	2.0
Dihydroxypropane g	4.0	4.0	4.0	4.0
Benzyl alcohol g	1.4	1.4	1.4	1.4
Dimethyl carbonol g	2.0	2.0	2.0	2.0
EDTA g	0.05	0.05	0.05	0.05
Methyl-p-hydroxybenzoate g	0.15	0.15	0.15	0.15
Propyl-p-hydroxybenzoate g	0.03	0.03	0.03	0.03
20% w/v NaOh g	4.0	4.0	4.0	4.0
Distill. H_2O q.s. to g	100	100	100	100

TABLE IV

Chemical and chemico-physical properties of the depolymerized deoxyribonucleic acids used in the formulations set out in Table III.

analytical parameters		Batch A	Batch B	Batch C
Phosphorus	(+)	8.62	8.25	8.90
Deoxyribose	(+)	19.0	20.4	22.3
Adenine	(+)	10.0	10.1	9.6
Guanine	(+)	9.3	8.5	8.4
Cytosine	(+)	7.0	6.5	6.5
Thymine	(+)	10.5	9.7	9.4
$\frac{A + G}{T + C}$	-	0.93	0.97	0.95
Molecular weight		18,000	43,000	29,000

(+) the data refer to the corresponding percentages in weight of the dry product.

TABLE V

Results relating to the effect of topical applications of preparations containing as active ingredients nucleic acids with the properties given in Table I, on rats in which surface capillary fragility was induced experimentally by administration of the Charlier diet for 21 days prior to the start of the trial. The applications were continued for 7 consecutive days, determining capillary resistance according to the Lavollay technique, before beginning topical applications and at the end of treatment. The results below are expressed in mm Hg (Mean ± S.E.)

GROUP (Ref. Tab. II)	(1)	(2)	(3)	(4)
A	319.6 ± 6.7	320.6 ± 7.2	1.0 ± 5.0	0.3
B	163.3 ± 3.6	169.0 ± 5.5	5.7 ± 5.9	3
C	166.5 ± 6.5	175.0 ± 14.4	8.5 ± 14.0	5
D	169.8 ± 6.4	212.5 ± 11.0**	42.7 ± 11.5**	25
E	172.8 ± 5.2	237.5 ± 5.3**	64.7 ± 5.9**	37
F	183.0 ± 11.9	277.0 ± 10.7**	94.0 ± 12.7**	51
G	172.0 ± 5.0	209.0 ± 14.2**	37.0 ± 9.7*	22

(1) Capillary resistance before start (zero time)

(2) Capillary resistance at end of trial

(3) Difference vs. zero time

(4) % variation vs. zero time

* = p = < 0.05 ** p < 0.01 Student's t-test vs. zero time

As confirmation of what was said previously regarding the common origin of the defects of the epidermis treated here, as regards "couperose" it should be noted that literature (S. Curri et al. "sostanze naturali ad azione sul microcirculo cutaneo" La Medicina Estetica Year 4 no. 1 January/March 1980) also demonstrates that capillary fragility is an important factor in the genesis of this particular phenomenon.

The efficacy of depolymerized deoxyribonucleic acids in reducing "couperose" on the face has been demonstrated with a test performed on 10 female subjects, aged between 13 and

59 years (average age 34 years). Subjects with phlogistic lesions of the face and those undergoing treatment with drugs ingested by the systemic route were excluded from the trial.

During experiments the formulation in example 2 was used. The active ingredient consisted of an equal-weight mixture of the batches of depolymerized nucleic acids given in Table IV. The applications were performed twice a day and were repeated for 60 consecutive days. Investigations were performed before the start and at the end of the experiments, by slide photographs, taken in standardised lighting conditions and using a macro lens, maintaining the focal length and the shutter opening constant. The photographs were taken in the morning, with the patient previously resting for twenty minutes in a room with controlled temperature and humidity.

The intensity of the colour of the epidermis revealed by the slide was then processed by means of a device for measuring colour intensity (Minolta Chroma Meter chromometer), set to measure the a* hemivector (chromometric coordinate drawn up by the International Lighting Commission in 1976), corresponding to the green-red spectrum.

In this way it was possible to estimate the quantity of red in the erythema.

In addition to the aforementioned instrumental parameter, a subjective evaluation of the evidence of reddening and the presence of dilated capillaries was also carried out on the basis of a score with the following points score system: 3 = highly evident, 2 = averagely evident, 1 = slightly evident. Table VI below gives the results obtained.

In order to further clarify the significance of the reduction in the a* parameter which was established at the end of the trial following treatment with the formulation containing the aforementioned depolymerized nucleic acids, it should be mentioned that the same parameter, determined out of a population of 91 healthy subjects, was 13.00. On the basis of Table VI, it can therefore be concluded that in this trial topical treatment with the aforementioned preparations gave rise to a significant improvement in the conditions of patients' faces.

TABLE VI

Reduction in "couperose" on the face due to the effect of topical applications of formulations containing depolymerized nucleic acids, repeated twice a day for 60 days. The values shown refer to the a* parameter and to the subjective evaluation of the reduction in "couperose" by means of the corresponding score. The determinations (Mean ± S.E.) were made before the start of treatment and after 60 days.

Parameter	Zero Time	After 60 days
a*	19.17 ± 0.36	15.96 ± 0.45 #
Subj. eval. (score)	2.50 ± 0.17	1.70 ± 0.15 #

# P < 0.01 Student's t-test

The efficacy of the preparations containing depolymerized nucleic acids in reducing cutaneous phenomena on the lower limbs as result of conditions of prolonged local fatigue, was demonstrated in a trial conducted on 30 female subjects, aged between 30 and 50 years (average age 40 years). All these subjects presented oedemas at the ankles with very evident and dilated surface capillaries on the lower limbs. In all the cases examined, these phenomena were accompanied by an aching and/or heavy sensation in the area of the limb concerned.

Treatment lasted 60 days. The daily topical application was performed on the whole limb. The composition of the formulation used in this trial is given in example 4. The active ingredient of the cream was composed of an equal-weight mixture of the three batches set out in Table IV.

The following parameters were evaluated before the start, at 30 and 60 days:

- subjective parameters: sense of heaviness
- objective parameters: oedemas at the ankles, presence of possible areas of skin pallour.

The evaluation of these subjective and objective parameters was performed by means of the score method, awarding a value, in arbitrary units, to the evidence of the phenomenon on the basis of the following scale: 0 = absent, 1 = slight, 2 = moderate, 3 = strong, 4 = very intense.

At zero time and at the end of the trial a capillaroscopic investigation of the ankle (lower third of leg, regio cruris medialis 5 cm above the internal malleolus) was performed using a Wild-MS-C instrument connected to a camera.

Study of the various photographs concerned the diameter of the capillaries and the number of loops and the presence of possible microhaemorrhages. The extent of these findings was evaluated by means of the score method awarding a value from 1 to 4, according to the following scale: 1 = worsened, 2 = original state, 3 = improved, 4 = much improved.

Measurement of the parameters described above was performed in the afternoon, so that the aforementioned cutaneous phenomena appeared with the normal evidence.
The results are give in Tables VII and VIII below.

TABLE VII

Value of the scores relating to the following clinical parameters: oedema, sensation of heaviness, areas of skin pallour, measured at zero time and after 30 and 60 days respectively (Mean ± S.D.).

Parameter	Zero Time	30 days	60 days
Oedema	0.9 ± 0.2	0.4 ± 0.1*	0.3 ± 0.1*
Heaviness	2.5 ± 0.1	1.3 ± 0.1*	0.7 ± 0.2*
skin pallour	0.8 ± 0.2	0.5 ± 0.1*	0.3 ± 0.1*

* $p < 0.01$

TABLE VIII

Modification in the amount of the average values of the scores relative to the overall evaluation of the capillaroscopic examination at zero time and after 60 days (Mean ± S.D.).

Parameter	Zero time	60 days
capillaroscopic analysis (scores)	2.0 ± 0.0	3.1 ± 0.1*

* $p < 0.01$

Tables VII and VIII show that at the end of the trial the improvement obtained following repeated topical applications of the above formulation, was statistically significant for all the parameters considered. It should be noted here, with reference to the capillaroscopic examination, that at the end of treatment the surface capillaries had almost disappeared, or at any rate had faded greatly, from the epidermis. The areas with oedema were fully resolved.

Example 1

Procedure for obtaining depolymerized deoxyribonucleic acids from a DNA of high molecular weight.
1 kg of DNA extracted from entrails is dissolved in 200 litres of deionised water at 70°C in which 27 kg of trihydrate sodium acetate and 30 kg of glacial acetic acid had previously also been dissolved. The solution is then heated at 70°C for 4 hours. Subsequently it is brought to

neutral pH with NaOH 5 N. It is then filtered obtaining 220 litres of solution. The depolymerized deoxyribonucleic acids are then precipitated by adding 24 litres of methanol (1.1 parts of solvent/1 part of solution). The precipitate is processed according to normal techniques, obtaining circa 650 g of product.
The analytical data relative to this preparation are the following (data in percentage of the dry product) : Phosphorous 8.74, Deoxyribose 18.3, Adenine 9.4, Guanine 7.8, Cytosine 7.2, Thymine 9.5, A + G / T + C = 0.88, molecular weight 58,000.

Example 2

ANTI-COUPEROSE CREAM

Depolymerized deoxyribonucleic acids	3 g
Propylene glycol	5 g
Tween 60	4.5 g
Span 60	3 g
Glyceryl monostearate	8 g
Isopropyl myristate	5 g
Perfume and preservatives	q.s.
Demineralized water	q.s to 100 g

Example 3

ANTI-CELLULITE CREAM

Depolymerized deoxyribonucleic acids	3 g
Polyethylene glycol stearate	9 g
Cetyl alcohol	5 g
Propylene glycol	5 g
Decyl oleate	10 g
Perfume and preservatives	q.s.
Demineralized water	q.s. to 100 g

Example 4

LEG CREAM

Depolymerized deoxyribonucleic acids	3.5 g
Ethoxylated fatty alcohols	7 g
Acetoglyceryl	8 g
Sorbitol 70%	5 g
Beeswax	4 g
Perfume and preservatives	q.s.
Demineralized water	q.s. to 100 g

Example 5

EYE CONTOUR CREAM

Depolymerized nucleic acids	4 g
Carbopol 940	1.5 g
Sodium hydrate	0.7 g
Glycerine	5 g
Perfume and preservatives	q.s.
Demineralized water	q.s. to 100 g

Example 6

LOTION FOR ASPHYTIC SKIN

Depolymerized deoxyribonucleic acids	1 g
Glycerine	5 g
N.M.F.	4 g
Perfume and preservatives	q.s.
Demineralized water	q.s. to 100 g

Example 7

SOOTHING OINTMENT

Depolymerized deoxyribonucleic acids	3 g
W/O self-emulsifier base	20 g
Almond oil	5 g
Propylene glycol	5 g
Perfume and preservatives	q.s.
Demineralized water	q.s. to 100 g

THE CLAIMS DEFINING THE INVENTION ARE AS FOLLOWS:

1. A method of reducing the unsightly defects of the epidermis of the face caused by " couperose " as herein before defined and/or to locally reduce, on the skin of the legs and ankles the defects which appear collaterally to a prolongued fatigue of lower limbs in an animal in need thereof, comprising the step of administering topically to said animal an effective amount of depolymerized deoxyribonucleic acids having the following analytical properties, expressed as percentage in weight of the dry product :

Phosphorous	8,0	-	9,6
Nitrogen	13,0	-	15,0
Desoxyribose	17,0	-	24,0
Adenine	8,0	-	11,0
Guanine	7,0	-	9,5
Cytosine	5,5	-	7,5
Thymine	8,0	-	11,0
$\frac{\text{Adenina + Guanina}}{\text{Thymine + Cytosine}}$	8,87	-	1,01
Molecular Weight (dalton units)	10.000	-	100.000

together with one or more cosmetically suitable vehicles and/or excipients.

2. A method according to claim 1 wherein said animal is a human.

3. A method according to claims 1-2, characterized in that said depolymerized deoxyribonucleic acids have a molecular weight of preferably between 15.000 an 60.000.

4. A method according to claims 1-3, characterized in that said effective amount of depolymerized deoxyribonucleic acids, expressed as percentage by weight of the composition, is between 0,5 % and 5 %.

5. A method according to claim 4, characterized in that said effective amount of depolymerized deoxyribonucleic acids,

expressed as percentage by weight of the composition, is between 1 and 4%.

6. A method according to anyone of the preceding claims characterized in that the compositions containing said effective amount of depolymerized deoxyribonucleic acids are in the form of creams, gels, ointments.

7. A method according to anyone of the preceding claims 1-6 for reducing unsightly defects of the skin and the body caused by "couperose" as hereinbefore defined.

8. A method according to any of the preceding claims 1-6 for reducing locally, on the skin of the legs and ankles, the unsightly defects which appear collaterally to prolonged fatigue of the lower limbs.

9. A composition when used in accordance with claim 1, substantially as hereinbefore described with reference to the examples.

DATED this 25th day of September, 1992.

CRINOS INDUSTRIA FARMACOBIOLOGICA S.P.A.
By its Patent Attorneys
DAVIES COLLISON CAVE