

AUSTRALIA
Patents Act 1990

655435

PATENT REQUEST: STANDARD PATENT / PATENT OF ADDITION

I / We, being the person(s) identified below as the Applicant, request the grant of a patent to the person identified below as the Nominated Person, for an invention described in the accompanying standard complete specification.

Full application details follow.

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Address

[54] Invention Title Product for the prophylaxis, diagnosis and
therapy of rheumatic, autoimmune, skin and
connective tissue diseases of an unknown aetiology,
[72] Name(s) of actual inventor(s) and methods of its manufacture and use.

..... Jara Ores RIHA

[74] Address for service in Australia PO Box 36, TENTERFIELD NSW 2372

..... Attorney Code

ASSOCIATED PROVISIONAL APPLICATION(S) DETAILS

[60] Application Number(s) and Date(s)

BASIC CONVENTION APPLICATION(S) DETAILS

[31] Application Number	[33] Country	Country Code	[32] Date of Application
.....

DIVISIONAL APPLICATION DETAILS

[62] Original application number

PARENT INVENTION DETAILS (Patent of Addition requests only)

[61] Application number Patent number

TICK IF APPLICABLE

I am an eligible person described in Sections 33 - 36 of the Act. ?

C012246 22/04/94
Drawing number recommended to accompany the abstract


(Signature)

29th August 1991
~~1-99~~
(Date)

COMMONWEALTH OF AUSTRALIA

Patents Act 1952

DECLARATION IN SUPPORT OF AN APPLICATION FOR A PATENT

(* Delete if inapplicable)

In support of the Application made by Jara Ores RIHA

A product for use in the prophylaxis, diagnosis and
for a patent for an invention entitled therapy of rheumatic, autoimmune, skin and connective
tissue diseases of an unknown aetiology, and methods of its manufacture and use.

I, Jara Ores RIHA
of PO Box 36, TENTERFIELD NSW 2372

do solemnly and sincerely declare as follows:-



*1. I am the applicant for the patent.
(or, in the case of an application by a body corporate)

~~*1. I am authorised by
the applicant for the patent to make this declaration on its behalf.~~

*2. I am the actual inventor of the invention.
(or, where a person other than the inventor is the applicant)

~~*2.
of
..... is the actual inventor of the invention and
the facts upon which * I am/* the is entitled to make the
application are as follows:-~~

Declared at Praha this twenty ninth day of August 1991

(Signature)

To: THE COMMISSIONER OF PATENTS



AU9184592

(12) PATENT ABRIDGMENT (11) Document No. AU-B-84592/91
(19) AUSTRALIAN PATENT OFFICE (10) Acceptance No. 655435

(54) Title
A PRODUCT FOR USE IN THE PROPHYLAXIS, DIAGNOSIS AND THERAPY OF RHEUMATIC, AUTOIMMUNE, SKIN AND CONNECTIVE TISSUE DISEASES OF AN UNKNOWN AETIOLOGY, AND METHODS OF ITS MANUFACTURE AND USE

International Patent Classification(s)
(51)⁵ A61K 033/26 A61K 009/06 A61K 009/08 A61K 009/12
A61K 009/70

(21) Application No. : 84592/91 (22) Application Date : 19.09.91

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(71) Applicant(s)
JARA ORES RIHA

(72) Inventor(s)
JARA ORES RIHA

(57) Claim

1. Product for the prophylaxis, diagnosis and therapy of rheumatic, autoimmune, skin and connective tissue diseases of an unknown aetiology, *characterized* in that it consists of a salt, or salts, of iron (Fe) and a lipid, or lipids, that had all been heated together in a stirred vessel to the boiling point of the composition at the atmospheric pressure in the presence of water which then may have been completely or partly removed by distillation from the product which is to be used for topical administration onto the human or animal skin as a means of preventing or diagnosing and/or arresting the development of systemic lupus erythematosus, vasculitis, sarcoidosis, amyloidosis, rheumatoid arthritis, osteoarthritis, rheumatic diseases, acne, comedos, papulopustular skin diseases, psoriasis, tinea, onychia, paronychia, corns, callosities, alopecia and indolent tropical ulcers.

DESCRIPTION

* Product for ~~use in~~ the prophylaxis, diagnosis and therapy of rheumatic, autoimmune, skin and connective tissue diseases of an unknown aetiology, and methods of its manufacture and use.

5

Technical field

This invention concerns the prophylaxis, diagnosis and therapeutic treatment of rheumatic, autoimmune, skin and connective tissue diseases of an unknown aetiology, and so it belongs to the realms of medical and veterinary rheumatology, immunology, immunopathology and dermatology.

10

Background art

The groups of diseases to which the present invention relates comprise a multitude of maladies, most of them being of an unknown or uncertain aetiology, many being chronic and intractable. Disadvantages and inadequacies existing in the state of art of prophylaxis, diagnosis and therapy of most of these maladies may be summed up as follows.

15

20

(a) It is not only that the causative agent (primary stimulus, persistent antigen) of most of these maladies has not been isolated nor identified, but hitherto it has not even been determined with certainty what type of microorganism, if any at all, is implicated as the aetiological agent. Numerous theories and hypotheses about the aetiology of rheumatic, autoimmune, skin and connective tissue diseases have held sway for varying periods of time. This situation may be exemplified by the following quotation: "... rheumatoid arthritis remains a mystery within a mystery ^{and still without a master...}" (Bywaters E.G.L., The recent, spectacular history of rheumatoid arthritis and rheumatology from about 1928 onwards as seen through English eyes - and a pair of

25

30

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Application No.84592/91, first amendments,
signed on 12th January 1992:

Jara Ores RIHA, applicant

spectacles. In Utsinger P.D. et al. (eds), Rheumatoid Arthritis, J.B.Lippincott Company, Philadelphia, 1985, p.5).

(b) Furthermore, hitherto it has not even been
5 known in which tissue or organ of the body the causative agent resides. Generally, the search for it has been focused on the tissues and/or organs showing clinical symptoms of the malady, e.g., on the joint in rheumatoid arthritis, while the apparently healthy parts of
10 the body were passed by.

(c) One of the consequences of an unknown aetiology of most rheumatic, autoimmune, skin and connective tissue diseases has been the uncertainty about their contagiousness, whether or not they can be transmitted
15 and by which routes and portals of entry, and how long the incubation or latent period can last.

(d) Hitherto, no effective prophylactic measures against most of these maladies have been available.

(e) Hitherto, it has been difficult, or impossible,
20 to diagnose most rheumatic, autoimmune, skin or connective tissue diseases at their very beginning or during their latent period twenty or thirty years before the onset of clinical symptoms.

(f) Hitherto, no remedy has been available capable
25 of eradicating the causative agent (primary stimulus, persistent antigen) of these maladies from the body and thus arresting the progress of the malady and curing the sufferer.

Hence, diverse medical treatments have necessarily
30 consisted mostly of a pain therapy and palliatives directed towards alleviation of symptoms, for example, anti-inflammatory drugs in rheumatoid arthritis, or restorative surgery using prostheses to replace destroyed joints.

35 In some skin diseases, the treatments have been aimed at what may be a superinfection of lesions with dermatophytes, as in tinea, or with bacterial flora,

as in acne. Such treatments usually do not eliminate the underlying cause of the clinical symptoms, that is the latency-reactivation sites embedded in the skin and the subcutaneous tissue very close to where a chronic fissuring or pustules occur.

Failing an unpredictable remission, many of the rheumatic, autoimmune, skin and connective tissue diseases have been considered practically incurable and as afflictions to be inevitably endured in old age by a portion of the population.

(g) Hitherto, it has not been recognized in theory, nor in practice, that most of the rheumatic, autoimmune, skin and connective tissue diseases may be linked by a common causative agent, a one which is capable of bringing about different clinical symptoms in different subjects depending on the genetic characteristics of their immune system and its history. For example, rheumatoid arthritis, acne vulgaris and tinea pedis have been regarded as aetiologically unrelated and unconnected diseases.

(h) Some of the systemic drug therapies can have adverse side effects and induce complications. For example, the use of anti-inflammatory drugs may lead to ocular complications: in case of corticosteroids, glaucoma may occur; in case of antimalarial agents, even blindness (Burke M.J., Ocular manifestations. In Utsinger P.D. et al. (eds), Rheumatoid Arthritis, J.B. Lippincott Company, Philadelphia, 1985, p.363).

30 Disclosure of the invention

The present invention aims to put an end to the elusiveness of the causative agent (primary stimulus, persistent antigen) that has been at the core of the difficulties experienced in the state of art of prophylaxis, diagnosis and therapy of rheumatic, autoimmune, skin and connective tissue diseases. For this purpose, in a practical manner, it provides a product,

as claimed in Claim 1, which consists of a salt, or salts,
of iron (Fe) and a lipid, or lipids, that had all been
heated together in a stirred vessel to the boiling point
of the composition at the atmospheric pressure in the
5 presence of water that subsequently may have been comple-
tely or partly removed by distillation from the product
which is to be used for topical administration onto the
human or animal skin as a means of preventing or diagno-
singing and/or arresting the development of systemic lupus
10 erythematosus, vasculitis, sarcoidosis, amyloidosis, rheu-
matoid arthritis, osteoarthritis, rheumatic diseases, acne,
comedos, papulopustular skin diseases, psoriasis, tinea,
onychchia, paronychia, corns, callosities, alopecia and indo-
lent tropical ulcers.

15 A salt of iron usable in accordance with the inven-
tion needs to have a physiologically harmless anion.
A highly water soluble ferric salt is preferred.

An usable lipid may be selected from physiological-
ly harmless fats, oils, waxes, phospholipids, glycolipids,
20 terpenes, steroids, cyclic acids and their esters,
mono- and polyhydroxy alcohols and their ethers, polymers
and copolymers of alkene oxides and their ethers. Prefer-
red among these are nondrying edible oils.

Said product is distinguished by its property of eli-
25 citing and curing lesions at asymptomatic latency-reacti-
vation sites in which resides the causative agent of rheu-
matic, autoimmune, skin and connective tissue diseases
while it evokes no such reaction in the rest of the skin.

For this purpose, said product may be used as it is
30 and applied directly to the human or animal skin. It may
also be incorporated as active ingredient into ointments,
creams, pastes, salves, gels, lotions, rinses, emulsions,
aerosol sprays, bath additives, washes, dispersions and
other compositions intended for a topical application to
35 the human or animal skin. In addition, said product may be
contained in devices which are to be applied to the human

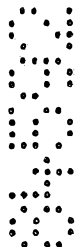




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or animal skin and which include pads, dressings, compresses, poultices, napkins.

Whichever way said product is applied to the skin, it has the effect of revealing by lesions it induces where
5 the latency-reactivation sites are, as well as curing the lesions and blocking the establishment of the causative agent in the skin, as claimed. The laten-



cy-reactivation sites are in many cases asymptomatic, and so the skin may appear and feel quite normal prior to a topical treatment with said product notwithstanding it may harbour hundreds of these sites.

5 The latency-reactivation sites, in which the causative agent can persist for years and decades of the host's life, are disseminated segments of the skin and the subcutaneous tissue frequently of a conical or wedge-like shape with the thin end pointing into the tissue
10 and the apex reaching an estimated maximal depth of about 15mm. The base of the cone lies at the skin's surface and it may be up to about 25mm in diameter, but of an estimated median diameter of about 7mm.

Frequently, the latency-reactivation sites are
15 found in intertriginous regions of the skin (commonly, one site being exactly opposite and in touch with another one which faces it), in wrinkles, furrows and skin folds, in the nail grooves and walls, in the hairy skin, the beard and the scalp.

20 In particular, the following skin regions are likely to harbour latency-reactivation sites: the skin of the toeclefts, the dorsum of the toes, the toenail grooves and walls; the skin of the dorsum of the feet, the shanks (especially around the ankles) and the knees;
25 the skin of the perineum, the groin, the genitalia (except the glans penis) and the perianal skin; the skin of the dorsum of the hands and the wrist, the nail grooves and walls; the skin of the back of the neck, the entire face (especially, the nose and the nostrils)
30 and the scalp. In addition, pimples, pustules, papules, macules, comedos, lentigines (freckles or "sunspots"), peeling, scurf, fissuring, itching, urticaria or prurigo, no matter how slight or insignificant these symptoms appear, may signal the existence of latency-reacti-
35 vation sites in the vicinal skin.

A characteristic feature of the distribution of latency-reactivation sites over the skin of the human body

is a pattern of an approximate bilateral symmetry. An important and consequential attribute of latency-reactivation sites is that they are embedded in the skin and the subcutaneous tissue, in some cases, overlain
5 by layers of thickened skin or enclosed in callosities. Furthermore, they have a conical root extending deep into the subcutaneous tissue, which is the part of the latency-reactivation site that can resist the eradication by said product for many months since it becomes
10 only slowly exposed at the skin's surface. The mechanisms operating in the growth of the latency-reactivation site and the reaction of surrounding tissue to it seem to converge into "burying" the site.

The necrosis of the latency-reactivation sites
15 brought about by a topical dermal application of said product proceeds from the surface of the skin into the subcutaneous tissue.

It is believed that the portals of entry of the causative agent are the hair follicles and openings in the
20 skin due to mechanical, chemical or enzymic injuries, and that after establishing itself in the skin, other cells in the vicinity are infected and the latency-reactivation site grows sending a root deeper into the tissue possibly to connect to a supply of nutrients
25 from a blood vessel.

Innovative solutions offered by the invention

(a) The present invention makes it feasible and practical to demonstrate that the causative agent of rheumatic, autoimmune, skin and connective tissue diseases
30 actually exists as it provides a product which in a topical dermal application provokes a reaction of the infected or transformed cells.

(b) The invention makes it possible to pinpoint the
35 sites in the skin where the causative agent asymptotically resides. This opens a new and seminal direction for its eventual isolation, identification and cultiva-



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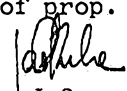
Innovative solutions offered by the invention

The novelty of the invention lies in combining a salt, or salts, of iron (Fe) with a lipid, or lipids; in applying the product topically with the aim at eliciting a reaction
5 in the skin of susceptible subjects; in associating the skin reaction with certain maladies (thus suggesting for the first time that they may have a causative factor in common); in recognizing that the skin reaction is an indicator and symptom of these maladies in their latent
10 period, and in making use of the skin reaction for their diagnosis and for arresting their further development.

(a) The present invention makes it feasible and practical to demonstrate that the causative agent of rheumatic, autoimmune, skin and connective tissue diseases actually
15 exists as it provides a product which in a topical dermal application provokes a macroscopic, clinical skin reaction at the site of infected or transformed cells.

(b) Consequently, the invention makes it possible to pinpoint the sites in the skin where the causative
20 agent asymptotically resides. This opens a new and seminal direction for its eventual isolation, identification and cultivation *in vitro*,




Riha, J.O., applicant

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~~tion in vitro~~, and for a more complete understanding of the aetiology and pathogenesis of rheumatic, autoimmune, skin and connective tissue diseases.

5 (c) The existence, the character and the distribution of the latency-reactivation sites, as they are revealed in the human skin by a topical dermal application of said product, strongly suggest that there is an infectious factor in the pathogenesis of most rheumatic, autoimmune, skin and connective tissue diseases
10 with a latent period lasting up to several decades.

(d) Said product when applied to the skin as claimed makes for the first time feasible an effective prophylaxis of rheumatic, autoimmune, skin and connective tissue diseases by blocking the establishment in the
15 skin of their, most probably ubiquitous, causative agent, its growth into the latency-reactivation sites and its spread by autoinfection to most parts of the integument. These processes may progress, waxing and waning, for decades with the effect of increasing the quantity
20 of antigen existing in the body and the magnitude of immune response to it, often accompanied by chronic fatigue.

(e) During the latent period of many of these maladies, while their causative agent is colonizing the skin and the latency-reactivation sites are tiny and
25 few, the clinical symptoms, which later are to overwhelm the patient, may be absent as, for example, in rheumatoid arthritis.

The present invention provides a product for the diagnosis of rheumatic, autoimmune, skin and connective
30 tissue diseases in their very early phase as well as for arresting their progress to a clinical stage. A periodical treatment of the skin with said product as claimed detects and eradicates in the initial stage of their growth the latency-reactivation sites which
35 may not betray their presence in any apparent way or only by trivial pimples or fissuring in the skin (now, however, revealed by this invention as being of impor-



tance).

Such diagnosis-cum-eradication of the latency-reactivation sites from the skin may have to be repeated at intervals throughout the lifetime of a person, especially if a genetic predisposition and living conditions favour the colonization of his/her skin by the causative agent.

(f) The therapy of rheumatic, autoimmune, skin and connective tissue diseases now being made possible by the present invention as claimed is radically different from the hitherto practised therapies insofar as they have been unable to target the aetiological agent which is now no longer inaccessible seeing that said product reaches it as it survives incognito in the skin and the subcutaneous tissue of the patient.

This invention provides a product for eliminating from the body the causative agent of maladies for which hitherto has been no cure.

From the sufferer's point of view, the fundamental difference is that managing a malady or treating its symptoms, instead of its cause, does not arrest its progress. From the medical science's point of view, the invention provides a new product which in an innovative step reveals that the primary stimulus or the persistent antigen is to be found in the skin - and not in those other organs which are showing clinical symptoms, such as, for example, the rheumatic joint.

(g) The present invention as claimed makes it feasible for the first time to demonstrate that many rheumatic, autoimmune, skin and connective tissue diseases have the same causative agent (primary stimulus, persistent antigen). Consequently, one of the innovative effects of the invention is that even mild skin ailments can no longer be regarded as having only a mere cosmetic or aesthetic importance.

(h) Considering the physiological properties of the ingredients from which said product is manufactured as

claimed, it is extremely unlikely that it could cause any harmful side effects. Furthermore, the invention does not comprise a systemic administration of said product: a local concentration of therapeutically active substances, sufficiently high for eliciting a reaction in infected or transformed cells of the latency-reactivation sites, is achieved through a topical dermal application. Nothing was observed which would suggest that the rest of the skin, apart from the latency-reactivation sites, reacts to the application of said product to it.

Advantageous effects of the invention

In addition to the innovative solutions which the invention offers in the field of the prophylaxis, diagnosis and therapy of rheumatic, autoimmune, skin and connective tissue diseases, other beneficial effects, such as the following ones, are expected to flow from its widespread use and industrial exploitation.

(a) The invention provides a product which is inexpensive to manufacture. This is a feature that should be of a particular benefit to the countries with scant resources enabling them to reduce their expenditure on imported medicines.

(b) In view of the enormous economic costs which the rheumatic, autoimmune, skin and connective tissue diseases inflict upon the humankind, if by using the present invention their prevalence was reduced even by a mere 1%, it would amount to a saving of hundreds of million U.S.dollars annually. For example, in the U.S.A. in 1979, the direct and indirect economic costs of rheumatoid arthritis alone were estimated at \$US4315 millions (Straszheim M., Economic costs. In Utsinger P.D. et al. (eds), Rheumatoid Arthritis, J.B.Lippincott Company, Philadelphia, 1985, pp. 854-855).

(c) As the invention offers a product and a method of its application useful in the study of epidemiology

and pathogenesis of maladies transmitted from the skin to the skin, it may contribute to the elucidation of the epidemiology and latency of Herpesviridae , HIV-1 and HIV-2.

5 (d) The invention by providing a product and a method of its use in detecting and eradicating slow-growing, often asymptomatic, latency-reactivation sites, may open a new line of investigation into oncogenes, latency and carcinomas.

10 (e) One of the effects of the invention may be to draw attention to the microbiology of the skin which, although it is an easily and directly accessible organ, might have been rather overlooked.

15 There are indications that the microorganisms inhabiting the skin, especially around the body orifices, have a greater influence upon their host's health than has hitherto been realized. For example, the incidence and severity of respiratory ailments may be affected by the latency-reactivation sites and microbial population
20 found around the lips and the nostrils.

25 It is very likely that the application of said product, in addition to eradicating the latency-reactivation sites, also alters the composition and density of the skin's microbial population with the result that it could improve the state of the patient's health in a number of yet unexpected ways.

30 (f) The invention provides a prophylactic, diagnostic, therapeutic and research tool for veterinary medicine.

Ways of carrying out the invention

35 The following examples describe the invention in further details and illustrate its practice but they are not limitative of the scope of the invention nor of the ambit of the claims.

Example 1

Manufacture of the product as claimed in Claim 1, ~~to 2~~.

Application No.84592/91, first amendments,
signed on 12th January 1992:

Jara Ores RIHA, applicant



A handwritten signature in dark ink, appearing to read "Jara Ores RIHA".

In a stirred vessel, fitted with a thermometer, con-
denser and a heating jacket, 150 grams of anhydrous
ferric chloride (FeCl_3) are dissolved in 4 litres of
water and 1 litre of sesame oil is added to the solu-
5 tion. The charge is heated under the atmospheric pres-
sure to its boiling point. The heat input is then ad-
justed to maintain a steady rate of distillation of
about 1 litre of distillate per hour. The distillation
is continued until the water content of the charge in
10 the vessel drops below 5% w/w. The distillate is dis-
carded. The residue in the vessel is the product as
claimed in Claim 1, ~~to 2~~.

Example 2

Preparation of a composition as claimed in Claim 2.
15 40 parts by weight of the product defined in
Claim ~~1 to 2~~ are blended with 60 parts by weight of a
pharmaceutically acceptable ointment base, such as
Simple Ointment, B.P.

Example 3

20 Manufacture of a therapeutic device as claimed in Claim 3.
A pad of cotton cloth, cut into a required size and
provided with a strip of adhesive bandage, is impreg-
nated with the product defined in Claim 1 or a composition according
to Claim 2 or a prophylactic or diagnostic preparation and/or a medicine according
to Claim 4 and packed in a disposable impermeable sleeve.

Example 4

The use of the product defined in Claim 1 ~~to 2~~
and of compositions and devices defined in Claim 2 to 4
which contain said product.

The invention to be effective requires that it is
applied to the subject's skin. This may be carried out
by using said product as it is, or a composition in
which said product is an ingredient, or a device con-
taining it and affixed to the skin so that said product
is allowed to come into contact with the skin. These
methods are not mutually exclusive and they may all be
employed simultaneously.

The choice is made according to what is a most con-



venient and practical method, having regard to the configuration of the skin region to be treated and the lifestyle of the subject. For example, generally, it would not be practical to apply pads onto the scalp or
5 the skin of the face where it is more convenient to use said product as it is or a cream in which said product is an ingredient. However, a pad or compress impregnated with said product and affixed to the skin by an adhesive bandage would be a good way of applying the invention to an indolent ulcer on the leg. From the point
10 of view of lifestyle, pads and compresses may suit a person confined to bed or in a sedentary occupation, but not someone who is physically very active.

Regardless of the way said product is applied onto
15 the skin, it is best to renew its application at least once a day after having washed the treated area of the skin with warm soapy water and debrided any lesions that may exist there.

An asymptomatic latency-reactivation site reacts to
20 a topical dermal application of said product by becoming apparent initially as a prurient or urticant spot, or a weal, pimple, pustule or papule which, in case of a larger site, usually develops into a, generally painless, ulcer. If a latency-reactivation site is very large or
25 if there is a cluster of them, the surrounding tissue may swell for a day or two when a lesion is about to appear or has just appeared.

The resistance of asymptomatic latency-reactivation sites to the treatment with said product vary widely:
30 in some sites, a reaction is brought forth in a few days, in others, it takes several weeks.

Once an ulcer is formed and debrided daily, it means that the objective of the present invention is being attained as the causative agent (primary stimulus, persistent antigen) of rheumatic, autoimmune, skin
35 and connective tissue diseases is being removed from the skin with the necrosed tissue of latency-reactiva-



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tion site. The application of said product, or a composition or device containing it, to the lesion is continued until it heals, which may take several weeks or months. Often, after it had healed, a pale scar remains
5 where previously was a latency-reactivation site. It resembles one caused by smallpox vaccination and it does not seem to tan.

The use of the present invention is adapted to the state of health of the subject. However, in most cases
10 it is best to treat one skin region after another, and not to apply the invention all over the entire integument simultaneously. The reason for this caution is to avoid, as far as possible, a syndrome of extreme fatigue, depression, loss of appetite and a sore throat
15 which may precede or accompany the onset of extensive skin ulceration resulting from a simultaneous reaction of many latency-reactivation sites to said product.

For each of the main categories of subjects, one may proceed as follows in applying said product or composition or a device which contains said product.
20

(a) When the invention is used for prophylactic or diagnostic purposes on a subject with no clinical symptoms, it is most fruitful to begin by treating, one by one, the regions which are the most prone to the colonization by the causative agent of rheumatic, autoimmune, skin and connective tissue diseases. The density of lesions elicited in one or two of these areas of the skin is a good indication of the extent of overall colonization.
25

The invention is consecutively applied to ^{the above-mentioned} ~~these~~ skin regions ^{where the latency-reactivation sites are to be found} ~~which are enumerated in this Description on page 5 (lines 14-35)~~, for about two weeks to each one, and lastly, the rest of the skin is treated. If no lesions are elicited, it may be provisionally interpreted that the area is free of the latency-reactivation sites. If many lesions appear in a skin region undergoing the treatment, it is best to wait before be-
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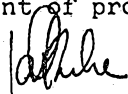


ginning to apply the invention to another part of the skin until the lesions that already erupted show signs of healing. Otherwise, one runs a risk of bringing forth many new lesions simultaneously, seeing that, when
5 treating an asymptomatic skin region, one does not know prior to applying the invention to it whether it will elicit clusters of many lesions or just a few lesions or none at all.

To effect the eradication of the latency-reactivation sites it is necessary to continue the application of the invention to the skin region under the treatment as long as any new lesions are being brought forth and/or the already elicited ones are not healed. As it may take months for some larger ulcers to heal, the treatment of the skin with the invention is pursued simultaneously in several skin regions in which lesions are
15 healing and/or a few new ones are still appearing.

This process of a progressive prophylaxis-cum-diagnosis and eradication of existing latency-reactivation sites is completed when the entire integument has been so tested. If in so doing, lesions have been elicited, then their number and size indicate the extent to which the subject's skin has been colonized by the causative agent of rheumatic, autoimmune, skin and
20 connective tissue diseases.

The diagnosis of asymptomatic latency-reactivation sites (by eliciting lesions at the sites) is a diagnosis of rheumatic, autoimmune, skin and connective tissue diseases in their latent phase. The interpretation of the findings is that the greater the number of lesions and their size (i.e., the greater the volume of infected or transformed cells), the higher is the probability that the subject will soon begin to present clinical symptoms of a rheumatic, autoimmune, skin or
30 connective tissue disease, unless some factor intervenes, slowing or arresting the growth and spread of the sites or causing them to regress.



Riha, J.O., applicant

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In the latent phase of these diseases, the subject may for years carry a burden of latency-reactivation sites in her/his skin. Since they are often asymptomatic and, in any case, hitherto not known to exist, and since their clinical symptoms as, for example, acneic pustules, have hitherto been related to some other cause or remained unexplained, the subject has hitherto not been aware of the burden she/he carries.

But, in many cases, the existence and proliferation of the latency-reactivation sites in the latent phase of rheumatic, autoimmune, skin and connective tissue diseases, is manifested by a recurrent or chronic fatigue and depression. Thus, even a partial eradication of the sites is likely to enhance the general well-being of the subject. ^{A further development of these maladies} ~~A total cure from these maladies~~ ^{is prevented} ~~in their latent phase is achieved~~ if their causative agent (primary stimulus, persistent antigen) is removed from the skin by eradicating all, or practically all, latency-reactivation sites from it.

(b) In cases of subjects suffering from a connective tissue (collagen, mesenchymal) disease, such as systemic lupus erythematosus in which antigen-antibody complexes injure blood vessels, or from vasculitis, or from sarcoidosis in which immunoglobulins are deposited in various organs, or from amyloidosis with hypergamma-globulinaemia and localized accumulations of amyloid, the same procedure for the use of the invention may be followed as when it is used for prophylaxis/diagnosis of latency-reactivation sites in the skin of subjects with no clinical symptoms.

(c) In cases of subjects suffering from rheumatoid arthritis, osteoarthritis or other rheumatic diseases, it may be best to apply the invention first to the skin over painful parts of the body, such as the joint, before proceeding to treat apparently normal skin regions as in cases of persons with no clinical symptoms. The reason for this is a probable nexus between an inflam-



John Riha
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med joint and the proximity of asymptomatic latency-re-
activation sites from where the causative agent (prima-
ry stimulus, persistent antigen) is repeatedly provok-
ing the immune response. If any latency-reactivation
5 sites are revealed close to the involved joint and era-
dicated, it may soon be felt in lessening of the in-
flammation and swelling of the joint.

In case of a painful hip joint, the relevant skin
regions comprise those of the perineum, the genitalia
10 and the groin and the perianal skin. In case of a pain-
ful knee, it is the skin of the knee and the shank.

It is necessary to be patient as it may be that it
will be progressively revealed that one's skin harbours
hundreds of latency-reactivation sites and that some of
15 them are quite large and deep. Such condition is most
likely to occur in elderly persons since it appears
that the causative agent takes many years to colonize
the skin so extensively. In these instances it may be
needed to carry on with the application of the inven-
20 tion to the skin for several years, perhaps with inter-
ruptions, as the roots of latency-reactivation sites
appear very slowly as if coming up from the deeper tis-
sue over many months.

However, a relief from rheumatic pain, swelling and
25 inflammation may be brought about by the application of
the invention a long time before a complete eradication
of the latency-reactivation sites from the skin is ef-
fected. A removal of even a part of necrosed latency-
reactivation sites is followed by abatement in the mag-
30 nitude of the immune response to the persistent antigen
and, consequently, the progress of the disease is re-
strained.

The eradication of the latency-reactivation sites
arrests the development of
~~brings the cure from~~ the disease in the phase it has
35 reached at that time, but injuries already caused to
the joints and/or other organs by the inflammatory me-
chanisms may be irreversible. Nonetheless, a body freed



from the latency-reactivation sites is a healthier one and thus more capable to repair at least some of the damage insofar as it is possible.


(d) In cases of subjects suffering from papulopustular skin diseases, e.g., acne, comedos and/or from psoriasis, tinea, onychia, paronychia, corns, callosities, alopecia, indolent tropical ulcers and/or other skin diseases, the application of the invention may best be directed first to the skin regions with clinical symptoms as latency-reactivation sites are likely to exist in their vicinity. The rest of the skin, which appears normal, may be treated later in the same manner as in cases of subjects with no clinical symptoms.

15 Forms of industrial exploitation of the invention

(a) The manufacture of the product as claimed ~~in Claim 1 to 2~~ and its packaging, marketing and distribution to hospitals, sanatoria, physicians, veterinarians, wholesale and retail pharmaceutical and veterinary medicine outlets, other manufacturers and/or its in-house use in manufacturing the compositions and devices as claimed, ~~in Claim 3 to 4.~~
~~2 to 5.~~

(b) The manufacture of the compositions and devices as claimed ~~in Claim 3 to 4~~ and their packaging, marketing and distribution to hospitals, sanatoria, physicians, veterinarians and wholesale and retail pharmaceutical and veterinary medicine outlets.




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THE CLAIMS DEFINING THE INVENTION ARE AS FOLLOWS:

5 1. Product for the prophylaxis, diagnosis and therapy of rheumatic, autoimmune, skin and connective tissue diseases of an unknown aetiology, *characterized* in that it consists of a salt, or salts, of iron (Fe) and
10 a lipid, or lipids, that had all been heated together in a stirred vessel to the boiling point of the composition at the atmospheric pressure in the presence of water which then may have been completely or partly removed by distillation from the product which is to
15 be used for topical administration onto the human or animal skin as a means of preventing or diagnosing and/or arresting the development of systemic lupus erythematosus, vasculitis, sarcoidosis, amyloidosis, rheumatoid arthritis, osteoarthritis, rheumatic diseases, acne, comedos, papulopustular skin diseases, psoriasis, tinea, onychia, paronychia, corns, callosities, alopecia and indolent tropical ulcers.

20 2. Composition for topical application onto the human or animal skin comprising the product according to Claim 1 in the form of an ointment, cream, paste, salve, gel, lotion, rinse, emulsion, aerosol spray, bath additive, wash or dispersion.

25 3. Device for topical application to the human or animal skin comprising the product according to Claim 1 or the composition according to Claim 2, such as a pad, a dressing, a poultice, a compress and/or a napkin.

30 4. Separate or combined prophylactic or diagnostic preparation and/or medicine and/or device for topical application onto the human or animal skin and/or for uses as claimed in Claim 1, *characterized* in that in the manufacture or making up or compounding of said preparation or medicine or device, was utilized the product of Claim 1 or composition of Claim 2 or device of Claim 3.



5 5. Use of the product according to Claim 1 or of
the composition of Claim 2 or of the device of Claim 3
or of the preparation and/or medicine of Claim 4 wherein
said product or composition or device or preparation
and/or medicine is/are used by way of a topical cutaneous
application and/or by the methods described on pages 11
to 17 of the present Specification for the prevention,
diagnosis and/or therapy of systemic lupus erythematosus,
vasculitis, sarcoidosis, amyloidosis, rheumatoid arthritis,
10 osteoarthritis, rheumatic diseases, acne, comedos, papulo-
pustular skin diseases, psoriasis, tinea, onychia, paron-
ychia, corns, callosities, alopecia and indolent tropical
ulcers.

15 6. Use of the product as defined in Claim 1 or of
the composition of Claim 2 or of the device of Claim 3
or of the preparation and/or medicine of Claim 4 in or
for testing said product, composition, device and/or
medicine on a live or dead human or animal body or organ
or tissue by way of a topical cutaneous application and/or
20 by the methods described on pages 11 to 17 of the present
Specification.

25 7. The product as defined in Claim 1 or the composi-
tion of Claim 2 or the device of Claim 3 to 4 or the
preparation and/or medicine of Claim 4, which is or are
utilized or employed in *in vitro* cultivation of human,
animal body tissues or fluids separated from the bodies
they originate from, or in research into the prophylaxis,
diagnosis, and/or therapy of systemic lupus erythematosus,
vasculitis, sarcoidosis, amyloidosis, rheumatoid arthritis,
30 osteoarthritis, rheumatic diseases, acne, comedos, papulo-
pustular skin diseases, psoriasis, tinea, onychia, paron-
ychia, corns, callosities, alopecia and indolent tropical
ulcers.



8. Culture medium or culture medium additive or ingredient, *characterized* in that the product as defined in Claim 1 or the composition of Claim 2 or the device of Claim 3 to 4 or the preparation and/or medicine of
5 Claim 4 was or is utilized in the manufacture or preparation or compounding of said culture medium or culture medium additive or ingredient.

9. Product for the prophylaxis, diagnosis and therapy of rheumatic, autoimmune, skin and connective tissue
10 diseases of an unknown aetiology as claimed in Claim 1, substantially as herein described with reference to the examples.



ABSTRACT

Product for the prophylaxis, diagnosis and therapy of rheumatic, autoimmune, skin and connective tissue diseases of an unknown aetiology, and methods of its manufacture and use.

5 The product is manufactured by heating together a salt, or salts, of iron (Fe) and a lipid, or lipids. It is for topical cutaneous application as a prophylactic, diagnostic aid and/or remedy during the latent or clinical stage of systemic lupus erythematosus, vasculitis, sarcoid-
10 osis, amyloidosis, rheumatoid arthritis, osteoarthrosis, acne, comedos, psoriasis, tinea, onychia, paronychia, corns, callosities, alopecia and indolent tropical ulcers. The novelty of the invention lies in the ability of the said product to elicit a skin reaction at the latency-
15 reactivation sites where the causative agent of the above-mentioned maladies resides, while bringing on no such reaction in the rest of the skin. Hitherto it has not been known nor used in the art that such composition of matter applied onto the skin of susceptible subjects
20 can at first elicit pustules, papules and/or weals, then heal resulting ulcers, and that with their débriding and the removal of the necrosed tissue of the latency-reactivation sites it is feasible to eradicate the causative agent (primary stimulus, persistent antigen) from
25 the skin, thus healing the lesions and arresting the development of these maladies at that particular stage. The said product may also prove useful in research into the above-mentioned and other maladies, and in *in vitro* cultivation of human, animal, plant or bacterial cells,
30 and viruses. The skin reaction the said product can elicit serves as an indicator of the above-mentioned maladies during their asymptomatic latent period.

