MANUKA OIL EXTRACT
LEPTOSPERMUM SCOPARIIUM

NOVEL FUNCTIONAL INGREDIENTS
FOR MULTI-PURPOSE FORMULATIONS
INDEX

CAMPO MANUKA EXTRACTS

CAMPO MANUKA OIL EXTRACT

CAMPO MANUKA AQUEOUS EXTRACT

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MATERIAL SAFETY DATA SHEETS

TOXICOLOGICAL & ECOTOXICOLOGICAL DATA

MATREX

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Manuka Extract

Leptospermum scoparium

Commonly referred to as Tea-tree, *Leptospermum* is distributed in Australia, South East Asia (i.e. the Malay Peninsula, Sumatra, Borneo, Java, Philippines, Sulawesi, Thailand, Flores, Moluccas, southern Burma and New Guinea) and New Zealand. Whilst *Leptospermum* occupies a variety of habitats from coastal dunes to high mountain peaks, it is most commonly found in wet or periodically wet substrates that are acidic and low in nutrient content.

*Leptospermum*. A rather small genus of shrubs or small trees of the family Myrtaceae, sub-family Leptospermoideae. It currently comprises 85 recognized species. The genus Leptospermum was first recognized by Johann Reinhold Forster and his son Johann Georg Adam Forster when they published the name *L. scoparium* Forst. & G. Forst in 1776.

To possess hard wood is a characteristic of the genus, and in those species which attain sufficient size it is useful for small objects. It is related that the aborigines of Australia use the wood of one for spears. Most of them are called 'Tea Tree' because their leaves can be made into a beverage like tea.

ETHNOBOTANY:

A very refreshing tea is made from the leaves, used for fever and lassitude. In the Moluccas, the mountaineers distil a little volatile aromatic oil from the plant, which they inhale for bronchitis and use as an embrocation for rheumatism. The oil was obtained from its leaves and twigs containing terpenes, particularly pinene, and citral. It extract has also been noted to ameliorate skin problems such as itchiness, rashes as well as accelerate healing of skin wounds and cuts. **Campo Manuka Extracts** are available in 3 types; an essential oil, an oil extract with ceramide and an aqueous extract. Both types exhibit anti-microbial properties, which is bacteriostatic. The oil extract is also applied in cosmetic formulations as colourings. It is ideal for body oils and emulsions made especially for sensitive skin.
**Technical Specification:**

**PRODUCT NAME:** CAMPO MANUKA OIL EXTRACT  
**OTHER NAME:** Leptospermum scoparium oil  
**PRODUCT NUMBER:** 97.129/63  
**SPECIES:** Leptospermum scoparium  
**INCI NAME:** Leptospermum scoparium Extract (Proposed) and Ceramide 3 oil  
**PLANT PARTS USED:** flowers (90%) and berries (10%)  
**APPEARANCE:** Clear, red, oil  
**ODOUR:** Characteristics  
**SPECIFIC GRAVITY:** 0.910 – 0.980  
**REFRACTIVE INDEX:** 1.430 – 1.465  
**VISCOSITY:** 25 – 35 (Mpa.s)  
**WATER CONTENT:** 010 max.  
**RECOMMENDED LEVEL OF USE:** 2–5%
## Technical Specification:

<table>
<thead>
<tr>
<th><strong>PRODUCT NAME:</strong></th>
<th>CAMPO MANUKA AQUEOUS EXTRACT</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>OTHER NAME:</strong></td>
<td>Leptospermum scoparium aqueous Extract</td>
</tr>
<tr>
<td><strong>PRODUCT NUMBER:</strong></td>
<td>97.129/67</td>
</tr>
<tr>
<td><strong>SPECIES:</strong></td>
<td>Leptospermum scoparium</td>
</tr>
<tr>
<td><strong>INCI NAME:</strong></td>
<td>Leptospermum scoparium Extract (Proposed)</td>
</tr>
<tr>
<td><strong>PLANT PARTS USED:</strong></td>
<td>flowers, leaves and berries</td>
</tr>
<tr>
<td><strong>APPEARANCE:</strong></td>
<td>Clear, dark red liquid</td>
</tr>
<tr>
<td><strong>ODOUR:</strong></td>
<td>woody aromatic</td>
</tr>
<tr>
<td><strong>pH:</strong></td>
<td>3.4 – 6.8</td>
</tr>
<tr>
<td><strong>SPECIFIC GRAVITY:</strong></td>
<td>1.010 – 1.090</td>
</tr>
<tr>
<td><strong>REFRACTIVE INDEX:</strong></td>
<td>1.370 – 1.445</td>
</tr>
<tr>
<td><strong>SOLUBILITY:</strong></td>
<td>Complete in water</td>
</tr>
</tbody>
</table>
Technical Specification:

PRODUCT NAME: CAMPO MANUKA ESSENTIAL OIL

OTHER NAME: Leptospermum Scoparium Floral Essence

PRODUCT NUMBER: 97.129/637

SPECIES: Leptospermum scoparium

INCI NAME: Leptospermum Scoparium Branch/Leaf Oil (Proposed)

PLANT PARTS USED: Leaves, Branches, Flowers

APPEARANCE: Clear, dark red, oil

ODOUR: Characteristics

SPECIFIC GRAVITY: 0.900 – 0.990

REFRACTIVE INDEX: 1.320 – 1.455
“(SAFETY DATA SHEET – compliant to GHS)”
CONFIRMS TO EC DIRECTIVE 91/155/EEC, EC REGULATION NO#1272/2008,
AMENDED EC REGULATION NO#790/2009 and Complies to The EU Cosmetic
Products Regulation (Regulation (EC) No 1223/2009) effective on July 2013., and to EU
Commission Regulation No.358/2014/9 of 9th April 2014 amending Annexes II and V, to
EU Regulation No No.1223/2009 of The European Parliament and of The Council on
Cosmetic products, (Effective Date 31st October 2014) AND to US DEPT.OF LABOR-
Occupational Safety & Health Admin directives and compliant to Globally Harmonized
System of Classification and Labeling of Chemicals (hereinafter referred to as “the
GHS”), and Complies and Confirms to the Requirements of State of California
Proposition 65.

A Quality Management System, compliant to the International Standard ISO 9001, was used to manufacture and test this material.

http://www.osha.gov/dsg/hazcom/ghs.html
http://www.unece.org/trans/danger/publi/ghs/ghs_welcome_e.html

| DATE OF FIRST ISSUE | February 18th 1992- Reviewer -
|                    | Dr Balasubramaniam PhD |
| DATE OF LATEST REVISION | Dec. 12th 1997- Rev’wer-
|                        | Dr Fergus Jes .G.Velasquez Bsc. Med Tech, MD |
|                        | February 10th 2012 – Reviewer=Joshua Teo|
|                        | February 5th 2013 – Reviewer –
|                        | Dr Balasubramaniam M, PhD |
|                        | 23rd March 2014 - Joshua Teo Balasubramaniam M PhD &
|                        | Oksana Nemchenko MD |
|                        | 12th February 2015 - Joshua Teo BSc. Chem, Balasubramaniam |
|                        | M PhD & Oksana Nemchenko MD |
|                        | 15th May 2016 - Joshua Teo BSc. Chem, Balasubramaniam M |
|                        | PhD & Oksana Nemchenko MD |

1 PRODUCT AND COMPANY IDENTIFICATION

COMMERCIAL NAME: CAMPO MANUKA ESSENTIAL OIL
OTHER TRADE NAME: Leptospermum scoparium floral oil essence
LATIN NAME: Leptospermum scoparium
INCI NAME: Leptospermum Scoparium Branch / Leaf Oil
China Translation 扫帚叶澳洲茶 (LEPTOSPERMUM SCOPARIUM) 枝/ 叶油
INTERNATIONAL CHEMICAL IDENTIFICATION (EC REGULATION NO#1272/2008 AMENDED NO#790/2009) and Compliant to the GHS:
MANUFACTURER: CAMPO RESEARCH Pte Ltd
(cGMP MFG. FACILITIES) Husdon Industrial Bldg., #05-02,
14, New Industrial Road, Singapore 536203

EMERGENCY TELEPHONE NUMBERS: (65)-3833631/(65)-3228503 (Singapore)

2 HAZARDS IDENTIFICATION

NOT CLASSIFIED AS DANGEROUS ACCORDING TO DIRECTIVE 67/548/EEC OR ITS AMENDMENTS.
HAZARD CLASS and CATEGORY CODE(s): DIVISION 1.6; NON-HAZARDOUS
PICTOGRAM: NONE
**HAZARD STATEMENT CODE(s)**

(EC REGULATION NO#1272/2008 AMENDED NO#790/2009) and compliant to the GHS

No GHS Pictogram (Totally Non-Hazardous Division 1.6: NO HAZARD STATEMENT

**GHS CLASSIFICATION:**

This material is Non-hazardous according To UN-GHS Criteria.

PICTOGRAM : NONE

No GHS Pictogram (Totally Non-Hazardous Division 1.6: No Hazard Statement.

**GHS LABEL ELEMENTS:**

No GHS Pictogram (Totally Non-Hazardous Division 1.6: No Hazard Statement.

---

### 3 COMPOSITION / INFORMATION ON INGREDIENTS

<table>
<thead>
<tr>
<th>100 PERCENT CARBON-DIOXIDE GAS EXTRACTED LEPTOSPERMUM SCOPARIUM -PLANT PARTS OIL SOLUBLE COMPONENTS</th>
<th>Leptospermum Scoparium Branch / Leaf Oil</th>
</tr>
</thead>
<tbody>
<tr>
<td>CTFA Monograph ID:</td>
<td>10572 – Leptospermum Scoparium Branch / Leaf Oil</td>
</tr>
<tr>
<td>CAS#</td>
<td>N/A – Leptospermum Scoparium Branch / Leaf Oil</td>
</tr>
<tr>
<td>CAS# EU</td>
<td>223749-44-8 (EU) – Leptospermum Scoparium Branch / Leaf Oil</td>
</tr>
<tr>
<td>CAS NO# (CAS Name)</td>
<td>223749-44-8 – Leptospermum Scoparium Branch / Leaf Oil</td>
</tr>
<tr>
<td>(EC REGULATION NO#1272/2008 AMENDED NO#790/2009) and compliant to the GHS</td>
<td></td>
</tr>
<tr>
<td>EINECS Name and Number</td>
<td>N/A – Leptospermum Scoparium Branch / Leaf Oil</td>
</tr>
<tr>
<td>EINECS# EU</td>
<td>N/A (EU) – Leptospermum Scoparium Branch / Leaf Oil</td>
</tr>
<tr>
<td>EINECS# (EINECS Name)</td>
<td>N/A (EU) – Leptospermum Scoparium Branch / Leaf Oil</td>
</tr>
<tr>
<td>(EC REGULATION NO#1272/2008 AMENDED NO#790/2009) and compliant to the GHS</td>
<td></td>
</tr>
<tr>
<td>EINECS Name and Number</td>
<td>Leptospermum Scoparium Branch / Leaf Oil</td>
</tr>
<tr>
<td>European Commission–Health &amp; Consumer Cosmetics–Cosing</td>
<td>Leptospermum Scoparium Branch / Leaf Oil – N/A (EU)</td>
</tr>
<tr>
<td>RISK PHRASES SAFETY PHRASES 25-26</td>
<td>None</td>
</tr>
<tr>
<td>GHS CLASSIFICATION: This material is Non-hazardous according To UN-GHS Criteria.</td>
<td>Not Mandatory</td>
</tr>
<tr>
<td>GHS LABEL ELEMENTS:</td>
<td>No GHS Pictogram (Totally Non-Hazardous Division 1.6: No Hazard Statement.</td>
</tr>
</tbody>
</table>

---

### 4 FIRST AID MEASURES

**EYE CONTACT:** Wash with water or standard eye wash solution. Seek medical advice, if irritation occur and persist.

**ORAL INGESTATION:** Edible in small quantities

**SKIN CONTACT:** Wash with water or shower.

---

### 5 FIRE FIGHTING MEASURERS

**COMBUSTIBLE AND PRESENTS NO SPECIAL FIRE HAZARD.**

**EXTINGUISHING MEDIA:** Treat as oil fire when store in HDPE drums with CO2, dry foam or dry chemical.

**PROTECTIVE EQUIPMENTS FOR** Standard Equipments.
### ACCIDENTAL RELEASE MEASURES

**ABSORB ONTO AN INERT MATERIAL**

AND **SCRAPE UP. REMOVE RESIDUE BY**

**SCRUBBING WITH HOT WATER OR**

**DETERGENT SOLUTION.**

### HANDLING AND STORAGE

**STORE IN SEALED CONTAINERS UNDER**

**NORMAL COOL, DRY WAREHOUSING**

**CONDITIONS.**

### EXPOSURE AND PERSONAL PROTECTION

**IN ACCORDANCE WITH GOOD**

**INDUSTRIAL PRACTICE AND HANDLING**

**USING STANDARD EYE PROTECTION.**

### PHYSICAL AND CHEMICAL PROPERTIES

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PHYSICAL FORM:</strong></td>
<td>Oil liquid</td>
</tr>
<tr>
<td><strong>COLOUR:</strong></td>
<td>Clear, Light to Dark Red</td>
</tr>
<tr>
<td><strong>ODOUR:</strong></td>
<td>Characteristic</td>
</tr>
<tr>
<td><strong>BOILING POINT:</strong></td>
<td>90 deg. Cent.</td>
</tr>
<tr>
<td><strong>MELTING POINT:</strong></td>
<td>-</td>
</tr>
<tr>
<td><strong>VISCOSITY:</strong></td>
<td>-</td>
</tr>
<tr>
<td><strong>FLASH POINT:</strong></td>
<td>-</td>
</tr>
<tr>
<td><strong>FLAMMABILITY SOLID/GAS:</strong></td>
<td>N/A</td>
</tr>
<tr>
<td><strong>AUTO FLAMMABILITY:</strong></td>
<td>N/A</td>
</tr>
<tr>
<td><strong>SPECIFIC REFRACTIVE:</strong></td>
<td>1.320 - 1.455</td>
</tr>
<tr>
<td><strong>EXPLOSIVE PROPERTIES:</strong></td>
<td>N/A</td>
</tr>
<tr>
<td><strong>pH:</strong> (1% in Oil Solution)</td>
<td>5.0 – 6.0</td>
</tr>
</tbody>
</table>

**Manuka Oil Constituents:**

- un-standardized sesquiterpenes
- un-standardized Trichetones
- un-standardized Flavesone

**PROPERTIES:**

- Anti-Bacterial, Perfumeries, antimicrobial, Chapped dry lips, Foot Care

**VAPOUR PRESSURE:**

N/A

**DENSITY:**

0.9000 -0.9800

**WATER SOLUBILITY:**

Insoluble

**OTHER SOLUBILITY:**

In Most Cosmetic Solvents

**BULK DENSITY:**

-?

**PARTITION COEFFICIENT:**

-?

**(OCTANOL/WATER)**

**EXPLOSIVE LIMITS:**

-?

### STABILITY AND REACTIVITY

THERMAL DECOMPOSITION:

Stable under normal conditions of use.

### TOXICOLOGICAL DATA

**ANIMAL TESTS:**

Last Done 1992, as requirements of the then **EC DIRECTIVE 91/155/EEC**

**ORAL:**

LD50 > 9,000 MG/KG (Body Wt.) Rat

Essentially Non-Toxic and Edible in Small Quantity.

**DERMAL:**

Expected To Be Essentially Non Toxic.

**INHALATION:**

N/A

**SPECIFIC CONCENTRATION LIMITS**

**M-FACTORS**

(**EC REGULATION NO#1272/2008 AMENDED NO#790/2009**) compliant to the GHS.

9,000 MG/KG (Body Wt.); CATEGORY 5

Essentially Non-Toxic and Edible in Small Quantity.

**TOXIC EFFECTS:**

**SKIN:**

Primarily Irritation Index (PII) = 0.0 ( Non-Irritating - Skintex ), Not A Primarily Irritant.

Non-irritant / Non-sensitizer as per Repeated Patch Insult Test on 50 Human volunteers.

Human Repeated Patch Test 48 hours:
**EYE:**

50/50 completely non-irritating / non-erythema causing **ingredient at 10% concentrate in water** on 50 human volunteers
Very Mild/Minimal-not A Transient Conjunctival Irritant at 10% concentrate in water(Eyetex Classification).

Summarized toxicological data as shown here are formation bounded under Non-Disclosure Agreement with various clients as when these Toxicological Data were established or their exclusive uses.

<table>
<thead>
<tr>
<th>12 ECOLOGICAL INFORMATION</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>BIODEGRADATION:</strong></td>
<td>Expected To Be Ultimately Biodegradable.</td>
</tr>
<tr>
<td><strong>FISH TOXICITY:</strong></td>
<td>No Data</td>
</tr>
<tr>
<td><strong>BACTERIAL &amp; VIRAL TOXICITY:</strong></td>
<td>No Data</td>
</tr>
<tr>
<td><strong>WGK CLASS:</strong></td>
<td>WGK (Self Classification)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>13 DISPOSE CONDITIONS</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>DISPOSE OFF ACCORDING TO A RECOGNISED METHOD OF CHEMICAL WASTE DISPOSAL.</strong></td>
<td></td>
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</table>

<table>
<thead>
<tr>
<th>14 TRANSPORT INFORMATION</th>
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</tr>
</thead>
<tbody>
<tr>
<td><strong>UN NUMBER# :</strong></td>
<td>N/A</td>
</tr>
<tr>
<td><strong>UN NAME:</strong></td>
<td>Not Assigned</td>
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<tr>
<td><strong>IMDG CODE/CLASS:</strong></td>
<td>Not Hazardous</td>
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<tr>
<td><strong>IMDG CODE PAGE NO.</strong></td>
<td>N/A</td>
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<tr>
<td><strong>ICAO/IATA AIR CLASS:</strong></td>
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<tr>
<td><strong>ICAO/IATA AIR CLASS PACKING GROUP:</strong></td>
<td>N/A</td>
</tr>
<tr>
<td><strong>RID/ADR CLASS:</strong></td>
<td>Non-Hazardous</td>
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<tr>
<td><strong>ADNR CLASS:</strong></td>
<td>Non-Hazardous</td>
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<tr>
<td><strong>LABELLING:</strong></td>
<td>No GHS Pictograms (Totally Non-Hazardous)</td>
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<tr>
<td><strong>PICTOGRAM SIGNAL WORD CODE(s):</strong></td>
<td>Division 1.6; No Hazard Statement</td>
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<tr>
<td><strong>HAZARD STATEMENT CODE(s):</strong></td>
<td>Similar Division 1.6; No Hazard Statement</td>
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<tr>
<td><strong>SUPPLEMENTARY HAZARD STATEMENT CODE(s):</strong></td>
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</tr>
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</table>

<table>
<thead>
<tr>
<th>15 REGULATORY INFORMATION</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>OCCUPATIONAL EXPOSURE LIMITS:</strong></td>
<td>N/A</td>
</tr>
<tr>
<td><strong>U.S. State of California Proposition 65 INGREDIENTS Presence</strong></td>
<td>None (Exempted from CA Prop 65 Register)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>16 OTHER INFORMATION</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>USES AS A COSMETIC ADDITIVE</strong></td>
<td>0.5 - 5.0 %</td>
</tr>
<tr>
<td><strong>This format and information is compiled by Kampoyaki Novel Natural Product Chemistry/ Novel Drug Discovery cGMP Labs Kobe, Japan; for Campo Research, Kyoto and Singapore.</strong></td>
<td></td>
</tr>
<tr>
<td>*<strong>Please take note that all specifications are liable to changes without prior notice.</strong></td>
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</tr>
</tbody>
</table>

CAMPO MANUKA OIL EXTRACT
THE ACTIVE NOVEL DRUG FOR THE COSMETIC FORMULATION
TOXICOLOGICAL & ECOTOXICOLOGICAL DATA

TOLERANCE
As to ensure a good level of innocuity Campo Manuka Oil Extract was tested in in-vitro as follows:

*Irritation potential of the chorio-allantoic membrane of an egg.
When tested on the chorio-allantoic membrane of a chicken egg, according to the technique developed by LUEPKE** in a 10% lipophilic soluble solution, Campo Manuka Oil is classified as non irritant.

*Cytotoxicity on human fibroblasts.
When tested on human fibroblasts using a method patented by BIOGIR (which can be applied to both hydro soluble as well as aqueous products), Campo Manuka Oil Extract in a 10% active aqueous phase or oily phase, does not show any signs of toxicity towards fibroblasts in culture.

* Eyetex
According to this technique, in a 10% active solution, Campo Manuka Oil Extract is classified non-irritant.

* Skintex
According to this technique, in a 10% active solution, Campo Manuka Oil Extract is non irritant. This tolerance data is confirmed by the tests carried out in vivo on health humans.

* Test on healthy humans
When patch tests were carried out at increasing concentrations (0.5%, 1.1%, 2.2%, 4.7%, 10% & 100%) on 50 subjects, Campo Manuka Oil Extract did not show any significant irritant reaction at all. Its tolerance is total satisfactory.

COMEDOGENESIS
Campo Manuka Oil Extract was tested in a 10% active solution on human volunteers, according to the usual protocols has proven to be free of comedogenic effect. Because of its good level of innocuity. Campo Manuka Oil Extract has proved to be first class natural bacteriostatic agent and skin moisturizer for various cosmetic formulae where tolerance is imperative (creams, lotions, moisturizer, etc.)

BIODEGRADABILITY
The ultimate aerobic biodegradability of Campo Manuka Oil Extract is measured according to STRUM TEST (OCDE 301 B, guideline EEC 84/449, Annex V. Method C5).
Under these conditions, a level of biodegradability of Campo Manuka Oil Extract is 100% in 28 days at 50 mg/ml.
The level of biodegradability of Campo Manuka Oil Extract is considered to be excellent.

Campo Research Singapore
Dec. 12th 1997
FINAL REPORT

DIVISION / COMPANY / GROUP: PROCTOR & Gamble
8700 Mason Montgomery Road
Box 1107, Mason, Ohio 45040
USA

ATTENTION: Lynn Mahony

TEST: The MATREX In Vitro Toxicity testing system
Salmonella Typhimurium Reverse Assay

TEST ARTICLE: * MANUKA OIL

EXPERIMENT REFERENCE NO: * 1997-12-13 A

Dr. Fergus Jes Velasquez, M.D.*.
Director of Microbiology

Dr. Balasubramaniam M, Ph.D.*
Laboratory Director

Date: Dec. 12th, 1997

This report is submitted for the exclusive use of the person, partnership, or corporation to whom it is addressed and neither the report nor the name of these Laboratories nor of any member of it's staff, may used in connection with the advertising or sale of any product or process without written authorization.

* Computer generated requires no signature
OBJECTIVE:

To evaluate the test article for irritancy potential utilizing the MATREX *in vitro* toxicity testing system.

INTRODUCTION

TESTSKIN and MATREX are sophisticated *in vitro* systems. Developed in Organogenesis Inc. of Cambridge, Massachusetts, they closely mimic human skin in structure and function. The Living Dermal Matrex (LDM) consist of a three-dimensional construct comprised of living cells in a collagen matrix. Nutrition is provided through the base via a permeable membrane, leaving the surface open to the atmosphere. This makes an ideal system for applying a variety of material, including liquids, powders, oils, gels and creams.

The Living Skin Equivalent (LSE) has all the features previously described, plus the formation of an actual epidermis complete with stratum corneum.

TESTSKIN and MATREX, when used with the recommended cell metabolism assay can quickly provide toxicological profiles. The procedure involves a solubilized, reactive tetrazolium salt (MTT), which is metabolized by the mitochondria of living cells and converted to purple formazan dye. The color intensity if the skin replica extract, measured photometrically, correlates directly with its viability. When measured against controls, values ranging from 0% to 100% (plus or minus approximately 20%) can be calculated for each dose of an applied substance.

Test Article:  
CAMPO MANUKA OIL  EXTRACT  
P# 97.129/63  B# 1997-12-13

Reference Articles:  
PROPYLENE GLYCOL & MORPHOLINE
METHOD:

The appropriate dilutions of test sample and control articles were applied to MATREX. After the appropriate exposure period, the articles were rinsed from the MATREX surfaces. MTT (tetrazolium salt) assay medium was utilized in order to quantify cell metabolism. At the end of the staining period, excised portions of each MATREX were immersed in acidified isopropanol which extracted the converted MTT from tissue samples. A Dynatech MR 4000 Automatic Microplate Reader was used to determine the absorbance of each extract at 570 nm. With the absorbance of a negative control defined as 100%, the percent absorbencies of the test and control articles were determined. The percentages listed below directly correlate with the cell metabolism in the MATREX samples.

RESULTS:

<table>
<thead>
<tr>
<th>Test Article</th>
<th>System</th>
<th>Percent Viability</th>
<th>Percent Inhibition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Campo Manuka Oil Extract</td>
<td>LDM</td>
<td>99.4%</td>
<td>0.6%</td>
</tr>
<tr>
<td>(100% - 1 hr.)</td>
<td>LDM</td>
<td>100%</td>
<td>0%</td>
</tr>
<tr>
<td>(1% - 1 hr.)</td>
<td>LDM</td>
<td>100%</td>
<td>0%</td>
</tr>
<tr>
<td>Propylene glycol</td>
<td>LDM</td>
<td>73%</td>
<td>27%</td>
</tr>
<tr>
<td>(100% - 1 hr.)</td>
<td>LDM</td>
<td>99%</td>
<td>1%</td>
</tr>
<tr>
<td>(1% - 1 hr.)</td>
<td>LDM</td>
<td>96%</td>
<td>4%</td>
</tr>
<tr>
<td>Morpholine</td>
<td>LDM</td>
<td>6%</td>
<td>94%</td>
</tr>
<tr>
<td>(100% - 1 hr.)</td>
<td>LDM</td>
<td>4%</td>
<td>96%</td>
</tr>
<tr>
<td>(1% - 1 hr.)</td>
<td>LDM</td>
<td>100%</td>
<td>0%</td>
</tr>
</tbody>
</table>

HISTORICAL IN VITRO RESULTS:
Propylene glycol has historically been categorized as virtually non-irritating when tested using the Draize irritation methodologies. Morpholine has been categorized as moderately irritating when in the same manner.

DISCUSSIONS:
The sponsor-submitted sample elicited in vitro results comparable to those recorded for propylene glycol.

CONCLUSION:
The results indicate that the sponsor-submitted product has virtually no irritation potential, under the conditions of this test.
CCR-Cytotest Cell Research

CCR PROJECT 95

SALMONELLA TYPHIMURIUM

REVERSE MUTATION ASSAY

REPORT ON
MANUKA OIL EXTRACT

Study Completion Date :
December. 12, 1997
CONCLUSIONS

The test article Campo Manuka Oil Extract was assessed for its potential to induce gene mutations according to the incorporation test (experiment I) and the preincubation test (experiment II) using Salmonella typhimurium strains TA 1553, TA 1537, TA 100 and TA 102.

The assay was performed in two independent experiments both with and without liver microsomal activation. Each concentration, including the controls, was tested in triplicate. The Campo Manuka Oil Extract was tested at the following concentrations:

33.3; 100.0; 333.3; 1000.0; 2500.0; and 5000.0 up/plate

No toxic effects occurred in the test groups with and without metabolic activation in experiment I and II in all strains used.

The plates incubated with the test article showed normal background growth up to 5000.0 up/plate with and without S9 mix in all strains used.

No substantial increases in revertant colony numbers of any of the five tester strains were observed following treatment with Campo Manuka Oil Extracts at any does level, either in the presence or absence of metabolic activation (S9 mix). There was also no tendency of higher mutation rates with increasing concentration in the range below the generally acknowledged border of significance.

A slight decrease (0.001%) in revertant colony numbers was observed in strain. TA 102 at 333.3 and 1000.0 up/plate in experiment I in the presence of metabolic activation. However, this effect is considered not to be relevant since it could not be reproduced in normally more sensitive pre-incubation assay.

Appropriate reference mutagens were used as positive controls and showed a distinct increase in induced revertant colonies.

In conclusion, it can be stated that during the described mutagenicity test and under the experimental conditions reported, the test article did not induce point mutations by base pair change of frameshifts in the genome of the strains used.
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