# Innovative Solid Lipid Nanoparticles-Enriched Hydrogels for Enhanced Topical Delivery of L-Glutathione: A Novel Approach to Anti-Ageing

**Speaker: Dr Mengyang (Marvin) Liu**
**Mentor: Professor Jingyuan Wen**

CRS 2025 ANNUAL MEETING & EXPOSITION
PHILADELPHIA, PA
JULY 13-18, 2025

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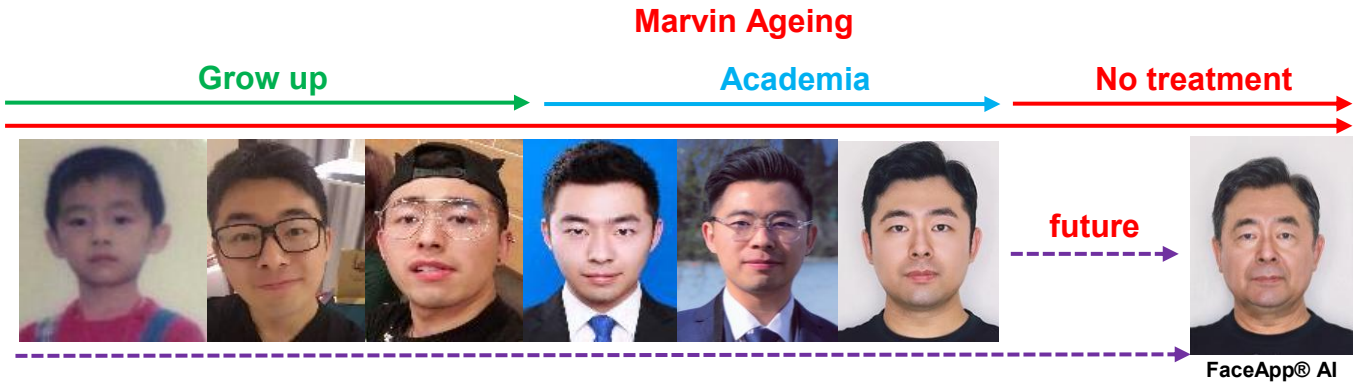
# Skin Ageing

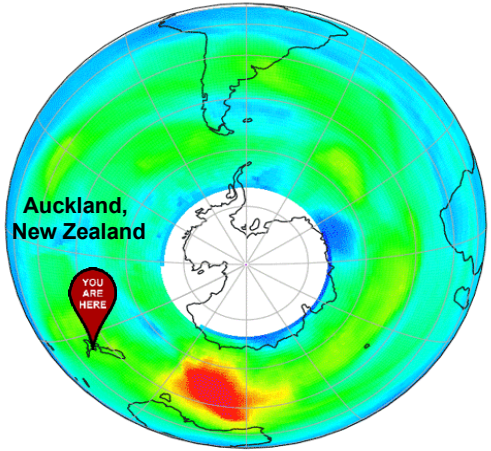
**Skin ageing**：a cumulative result from oxidation stress, influenced by both intrinsic (genetic and chronological) and extrinsic (environmental and lifestyle) factors

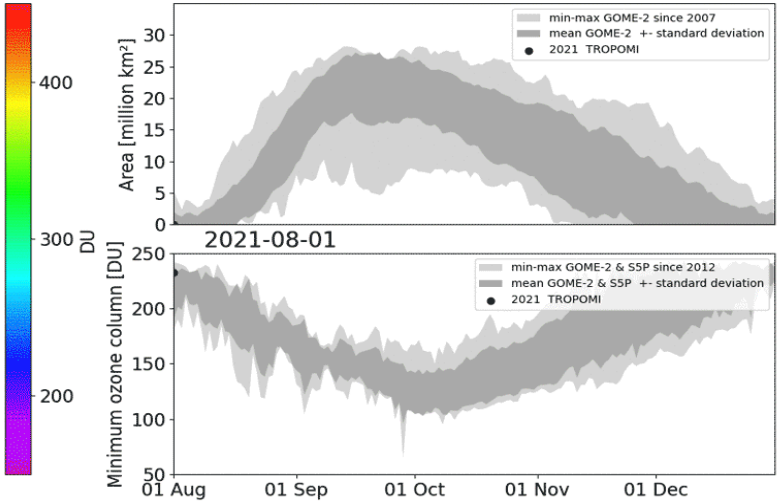


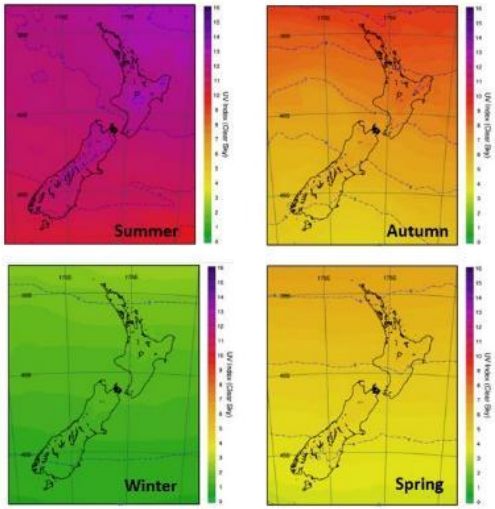
# UV Radiations in NZ

**Ozone hole (NZ)：** Less ozone conc. but more UV rays.

**UVA radiations**: Global Rank #2 New Zealand (UV index > 11)



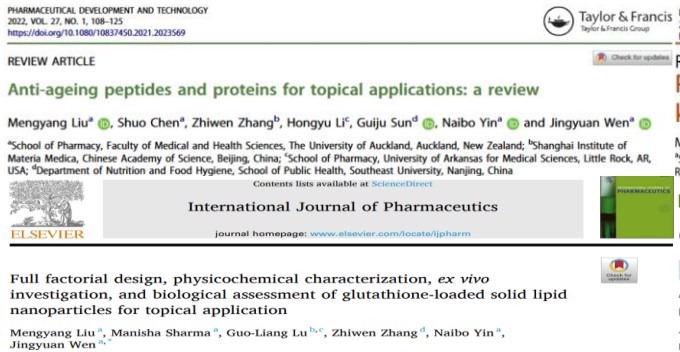



# Anti-ageing

**Anti-ageing peptides**

**Antioxidants**：inhibit the oxidation from reactive oxygen species (ROS)/free radicals.

**Glutathione (GSH):** “mother of all antioxidants”; endogenous tripeptide


PHARMACEUTICAL DEVELOPMENT AND TECHNOLOGY
2022, VOL. 27, NO. 1, 108–125
https://doi.org/10.1080/10837450.2021.2023569

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REVIEW ARTICLE

Anti-ageing peptides and proteins for topical applications: a review

Mengyang Liu[a], Shuo Chen[a], Zhiwen Zhang[b], Hongyu Li[c], Guiju Sun[d], Naibo Yin[a] and Jingyuan Wen[a]

[a]School of Pharmacy, Faculty of Medical and Health Sciences, The University of Auckland, Auckland, New Zealand; [b]Shanghai Institute of Materia Medica, Chinese Academy of Science, Beijing, China; [c]School of Pharmacy, University of Arkansas for Medical Sciences, Little Rock, AR, USA; [d]Department of Nutrition and Food Hygiene, School of Public Health, Southeast University, Nanjing, China

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ELSEVIER

Full factorial design, physicochemical characterization, *ex vivo* investigation, and biological assessment of glutathione-loaded solid lipid nanoparticles for topical application

Mengyang Liu [a], Manisha Sharma [a], Guo-Liang Lu [b,c], Zhiwen Zhang [d], Naibo Yin [a], Jingyuan Wen [a,*]


DRUG DEVELOPMENT AND INDUSTRIAL PHARMACY
2020, VOL. 46, NO. 5, 717–731
https://doi.org/10.1080/03639045.2020.1752708

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RESEARCH ARTICLE

Preformulation studies of L-glutathione: physicochemical properties, degradation kinetics, and *in vitro* cytotoxicity investigations

Mengyang Liu[a], Manisha Sharma[a], Guo-Liang Lu[b], Naibo Yin[a], Murad Al Gailani[a], Sree Sreebhavan[b] and Jingyuan Wen[a]

[a]School of Pharmacy, Faculty of Medical and Health Sciences, University of Auckland, Auckland, New Zealand; [b]Auckland Cancer Society Research Centre, Faculty of Medical and Health Sciences, University of Auckland, Auckland, New Zealand

RECORD ABSTRACT ARTICLE

Oral delivery of glutathione: antioxidant function, barriers and strategies

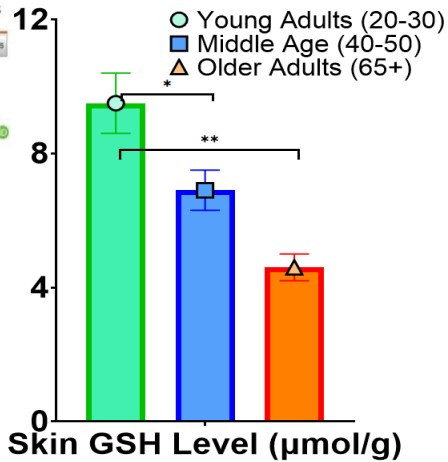
PUBLISHED REVIEW-ARTICLE

Author(s): Tielan Wei [a], Sachin Sunil Thakur [a], Mengyang Liu [a], Jingyuan Wen [a,*]

Publication date (Electronic): 10 May 2022

Journal: Acta Materia Medica

Publisher: Compuscript




# Any problems to deliver GSH in skin?

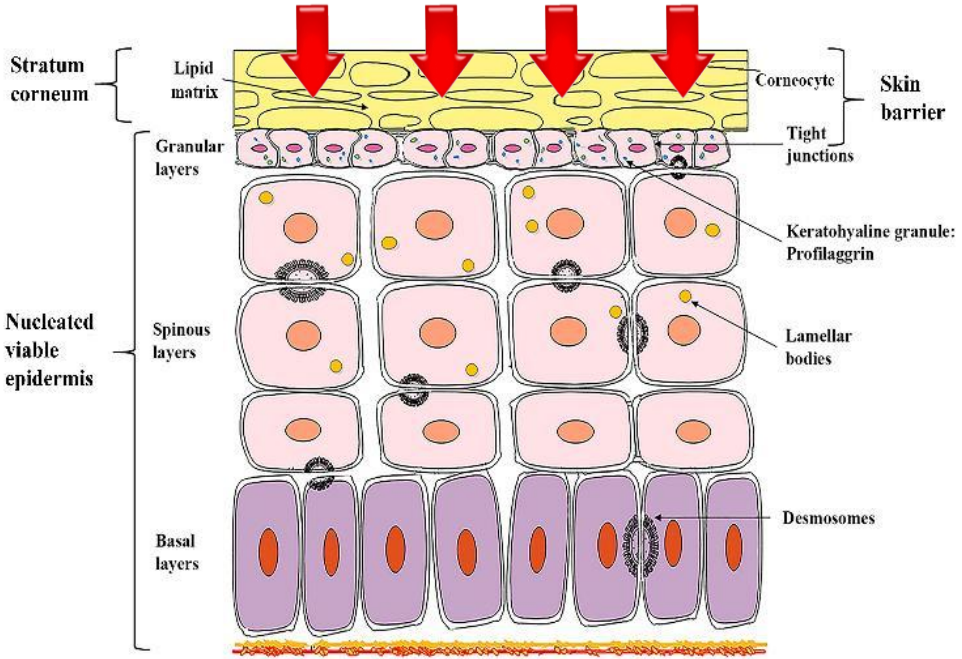
# Problem #1: Skin barriers

**Skin barriers**：

1) **Stratum Corneum (SC):**

2) **Tight junctions**

- Molecular weight: < 500 Daltons
- Log P (partition coefficient): 1 to 3
- High lipid solubility
- Low skin irritation



# Problem #2: GSH physicochemical properties

DRUG DEVELOPMENT AND INDUSTRIAL PHARMACY
2020, VOL. 46, NO. 5, 717–731
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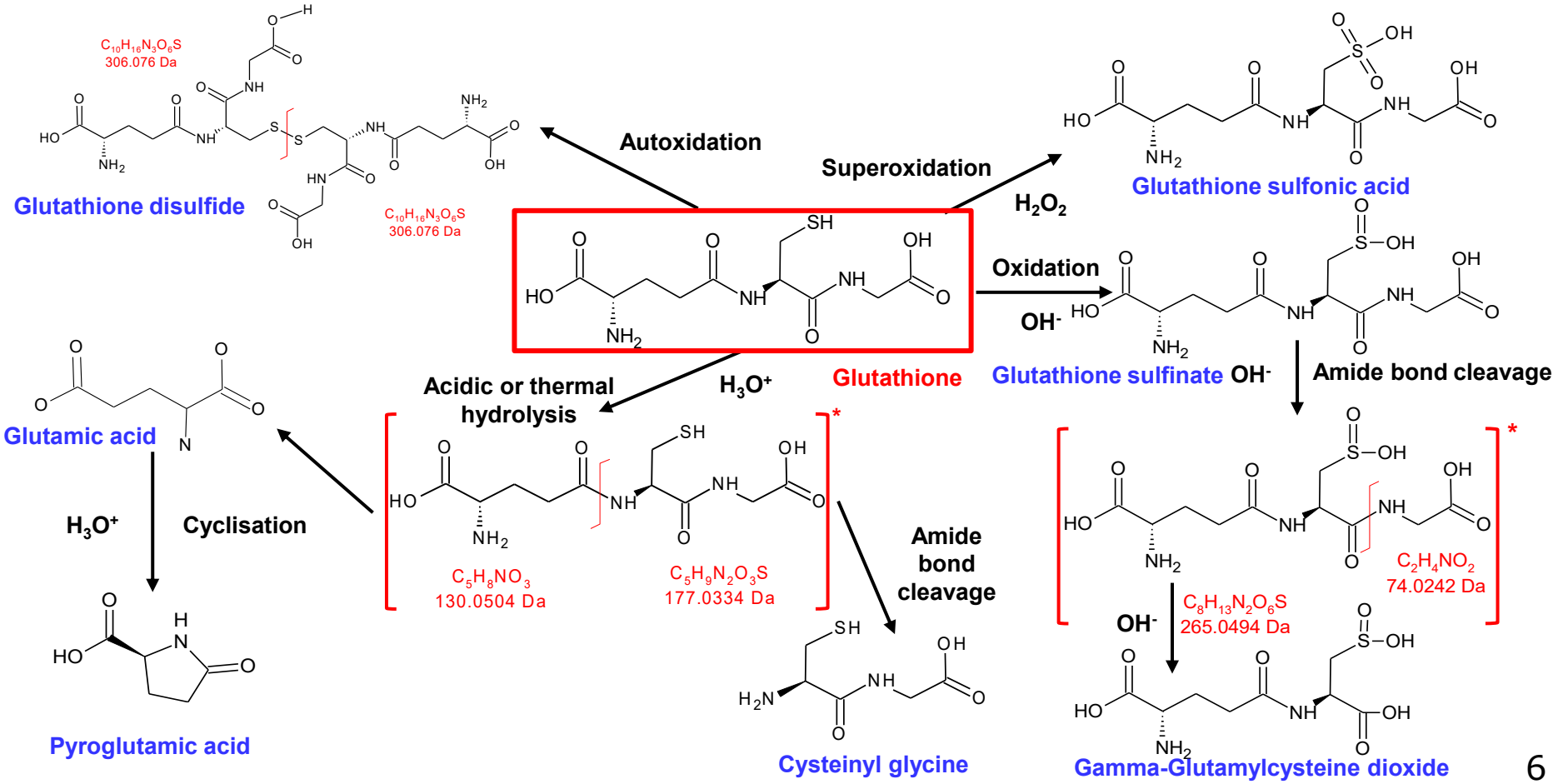
RESEARCH ARTICLE
Preformulation studies of L-glutathione:

Waipapa Taumata Rau University of Auckland



# Problem #3: Application on Skin

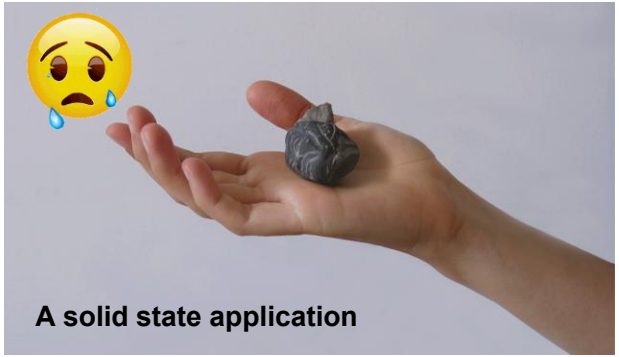
## Semi-solid dosage forms

Skin Retention & Applicable

- Ointments
- Creams
- Gels
- Others

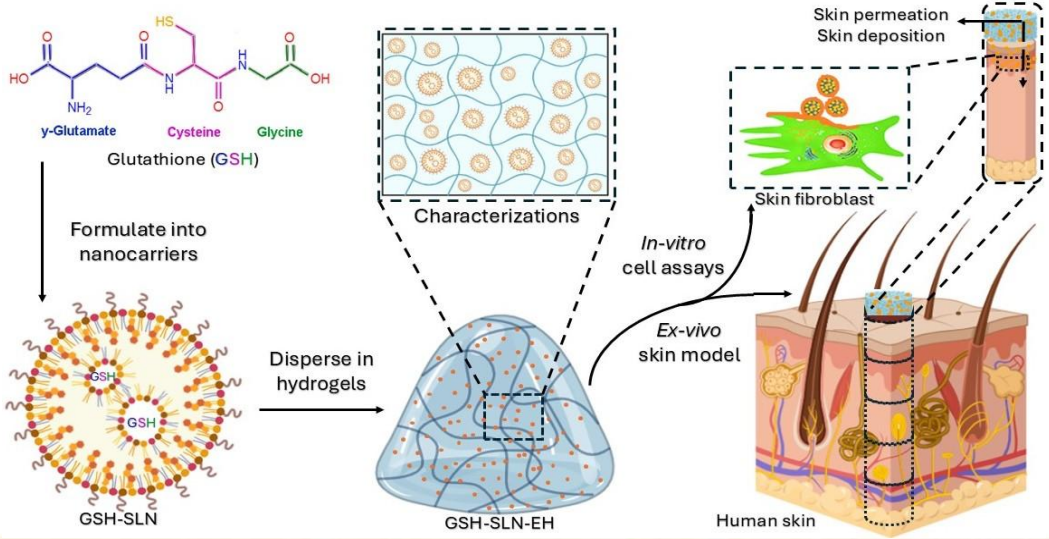
Hydrogel

- Cross-linked carrier
- Skin hydration
- Sustained release
- Biocompatibility
- Comfortable texture




# Aim & objectives

**Aim** to develop a SLN enriched hydrogel for topical delivery of anti-ageing GSH for skin ageing




## Objectives

- **Formulation development**
- **Formulation characterisations**
- ***In-vitro* cell studies**
- ***Ex-vivo* investigations**

# Formulation development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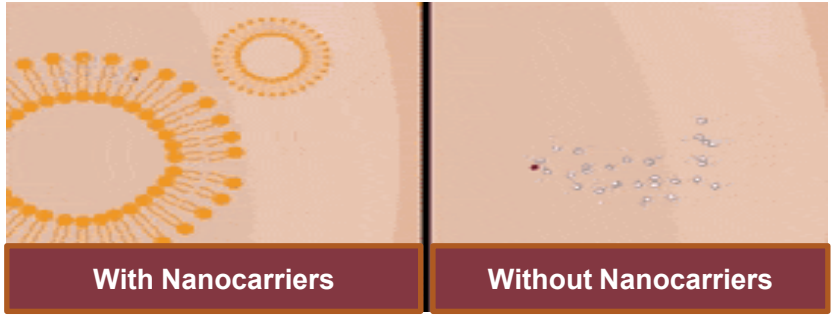
## Solid lipid nanoparticles (SLNs)

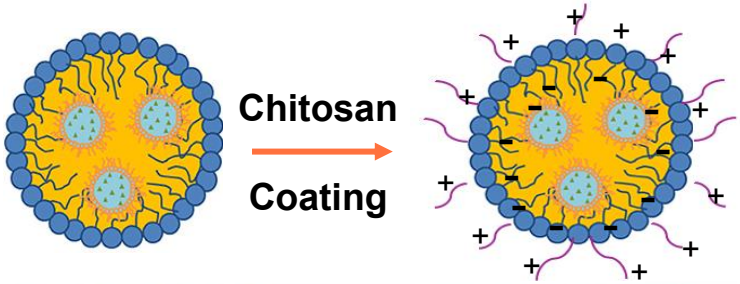
### To enhance penetration:

- Lipid based carrier system
- Particle size 50 to 300 nm
- Penetration: surfactants & chitosan
- Hair follicle transport




### To improve stability:

- Solid state
- Non/low-aqueous phase



# Formulation development

## Development of GSH-SLN

Contents lists available at ScienceDirect
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Full factorial design, physicochemical characterization, *ex vivo* investigation, and biological assessment of glutathione-loaded solid lipid nanoparticles for topical application

Mengyang Liu [a], Manisha Sharma [a], Guo-Liang Lu [b,c], Zhiwen Zhang [d], Naibo Yin [a], Jingyuan Wen [a,*]

Waipapa Taumata Rau University of Auckland

**Factors screening by $2^{5-1}$ fractional factorial design:** Particle size & EE%

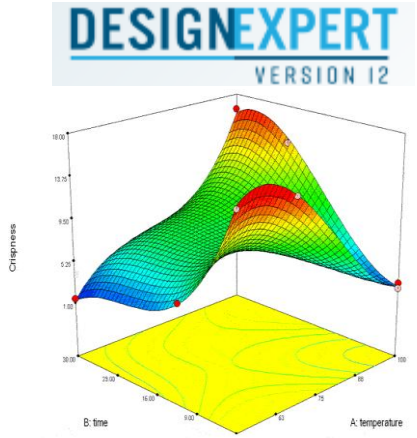
A: surfactants ratio (Span 85 : Tween 80)

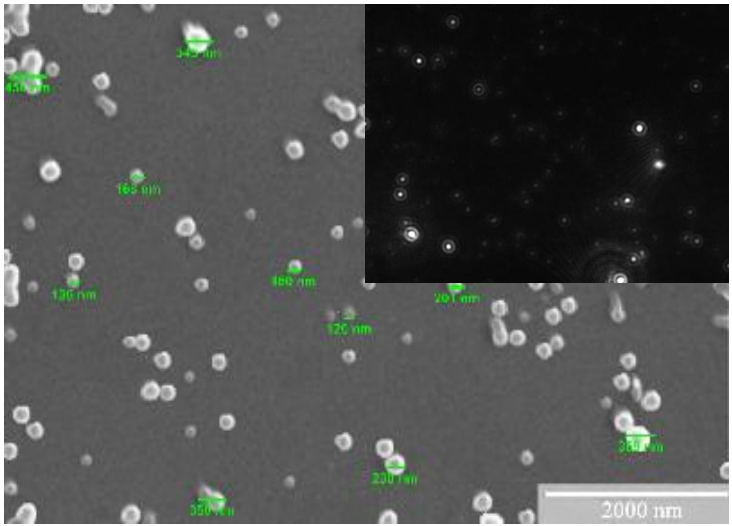
B: sonication time

C: concentration of chitosan

D: sonication amplitude

E: GSH concentration

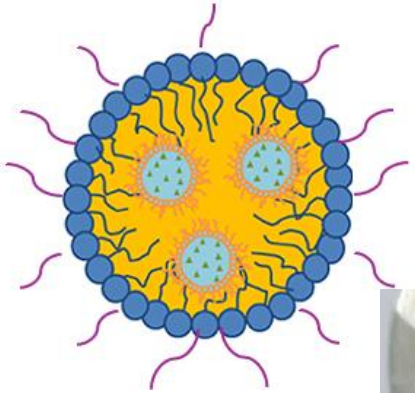


# Formulation development

## Development of GSH-SLN-EH

**GSH-SLN-EH preparation:** Carbopol® 971 (1%, 3%, and 5% w/v)

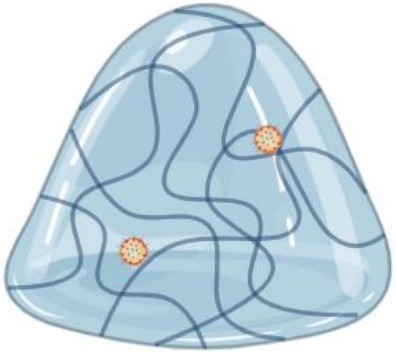


Enrich into

Stirring

Solidification

25℃



# Characterisation of GSH-SLN-EH

## GSH-SLN-EH

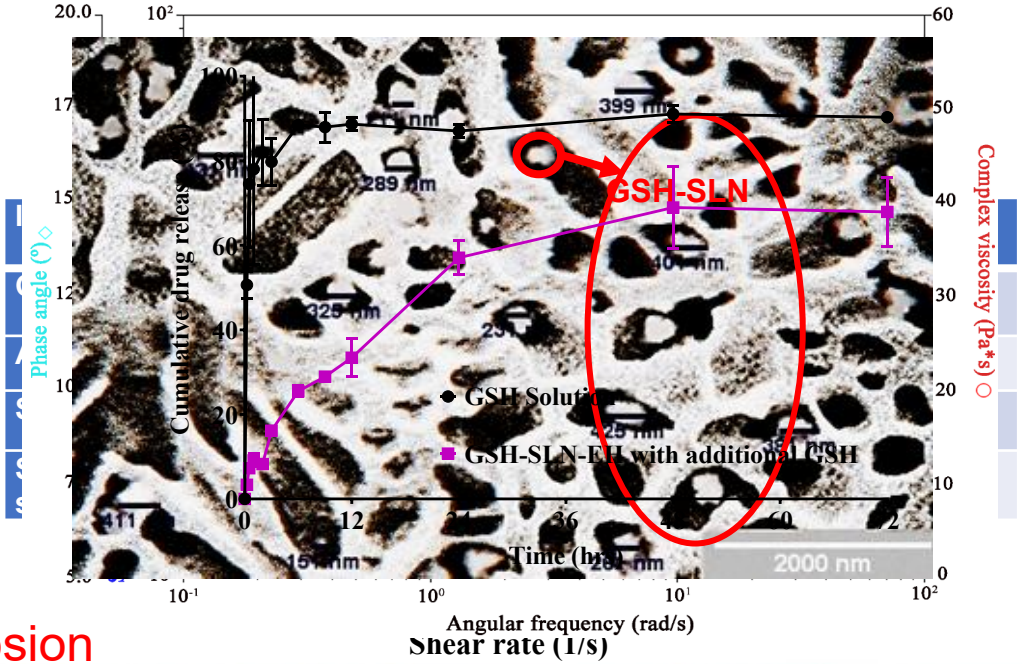
**Morphology: Cryo-SEM**
~1000 nm pore mesh size

**Texture profile:**

**Rheological properties:**
Pseudoplastic fluids

**Viscoelasticity:**
Solid-like to liquid-like transition

**Drug release & mechanism:**
Korsmeyer-Peppas:diffusion & erosion



# *In Vitro* Cell Culture Studies (Skin Fibroblast)

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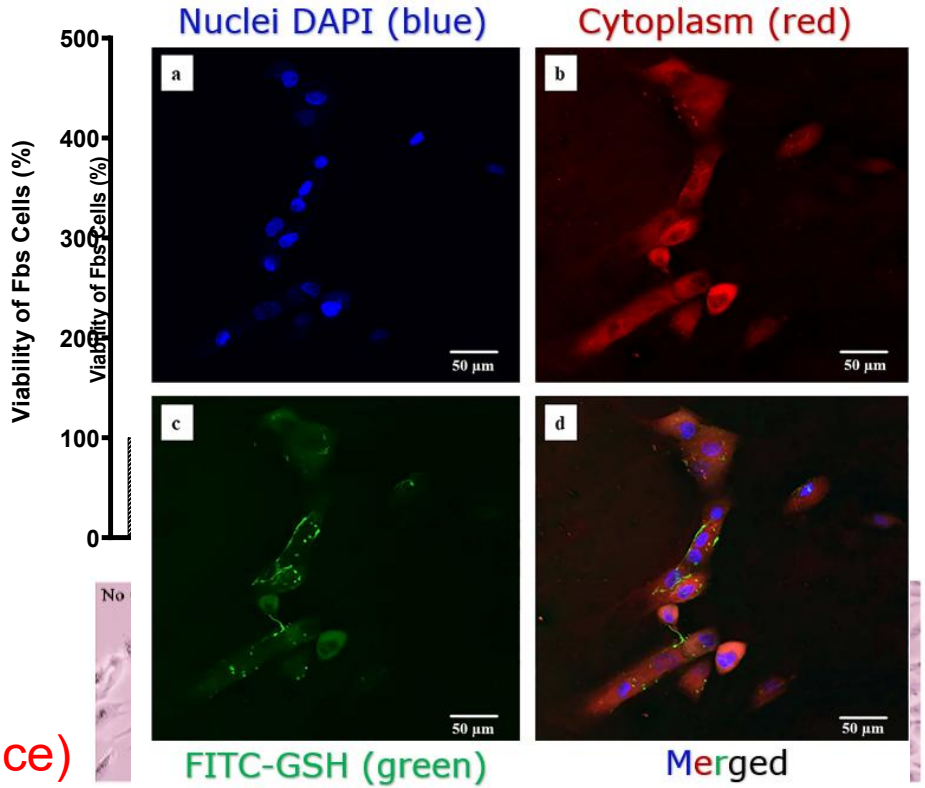
**Cytotoxicity:**
No cytotoxicity and cell proliferation

**UVA radiation rescue:**

**Antioxidant enzyme activities**
High levels in SOD and GSH-px

**Cellular uptake:**
Maximum at 2 hours
(<3 hours avoid skin enzyme clearance)

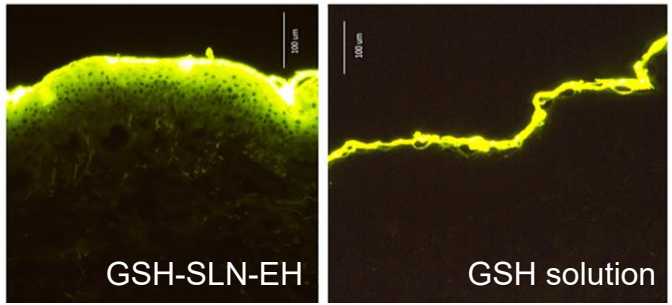


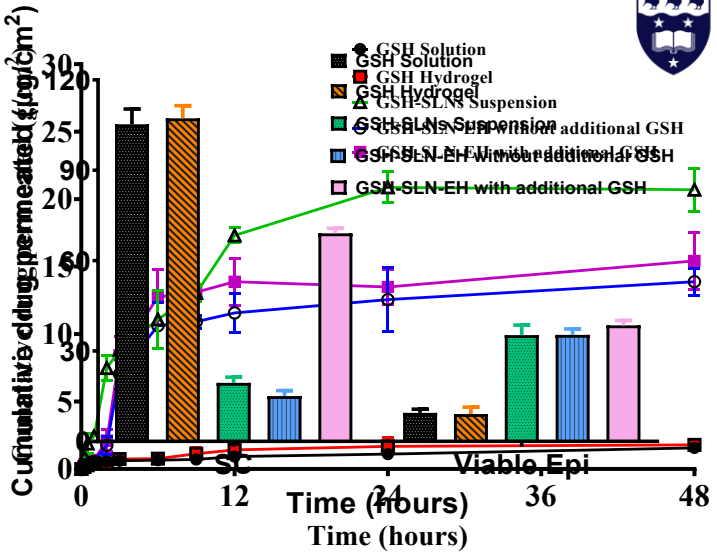
# *Ex Vivo* Studies (Human Skin)

**Skin integrity:**
28.4 ± 1.8 kΩ·cm² skin's TEER

**Permeation studies:**
GSH-SLNs highest permeation

**Deposition studies:**
GSH-SLN-EH highest Epi- deposition




| Formulations | SC deposition of GSH after 48 hours (µg/cm²) | Epi/dermis deposition of GSH after 48 hours (µg/cm²) |
|---|---|---|
| GSH solution | 105.3 ± 5.0 | 9.5 ± 1.2 |
| GSH gel | 107.2 ± 4.2 | 8.07 ± 2.3 |
| GSH-SLNs | 19.4 ± 1.9 | 33.3 ± 3.3 |
| GSH-SLN-EH | 15.0 ± 1.8 | 35.8 ± 2.0 |

# Conclusions



- **GSH-SLN-EH Formulation** was developed
- **Optimised formulation** was characterised
- ***In-vitro* cell and *ex-vivo* studies** were investigated

**The aim was achieved to topical delivery of anti-ageing GSH using SLN-EH**

- **Future perspectives**
- Industrial partnership & commercialisation
- *Quality control trails & GMP complained (scale up)*

# Acknowledgements





Maurice & Phyllis Paykel Trust

University of Auckland Faculty of Medical and Health Sciences Postdoctoral Society

CRS Australian Local Chapter Drug Delivery Australia Best Student Oral presentation Prize for CRS Travel Grant

QLD

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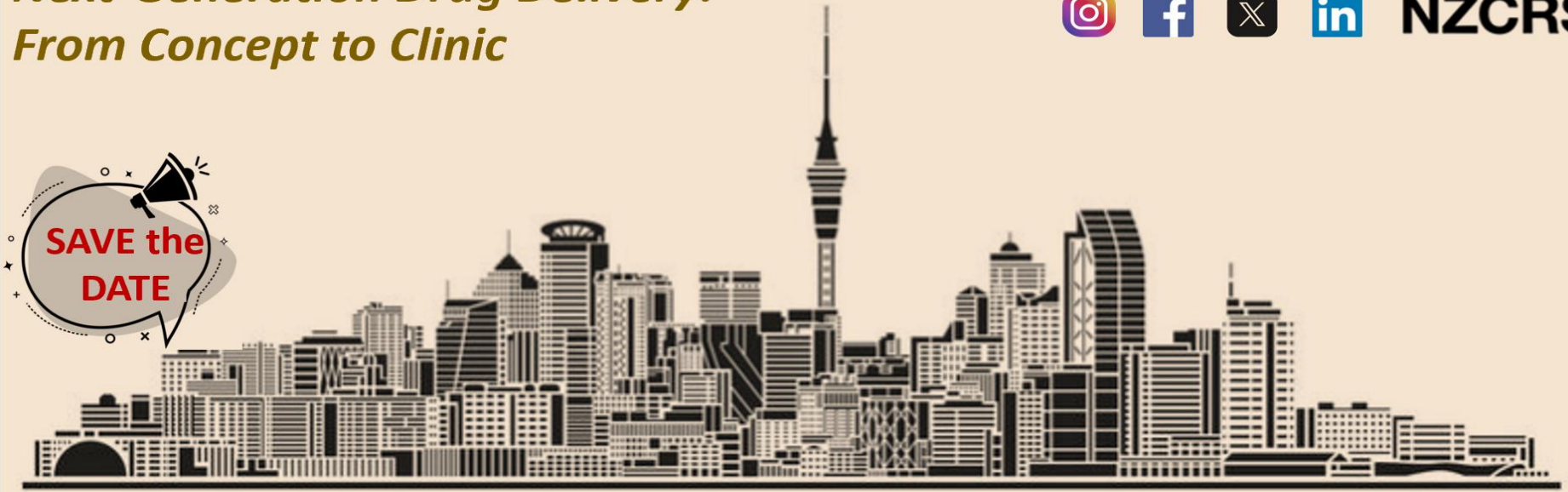

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# Optimised GSH-SLN

| Items | Values selected |
|---|---|
| Ratio of Span® 85 and Tween® 80 | 0.1 |
| Ratio of two sonication times | 0.5 |
| Concentration of chitosan polymer | 0.1 % |
| Sonication amplitude | 45 % |
| GSH concentration | 40. mg/mL |

# Stability studies

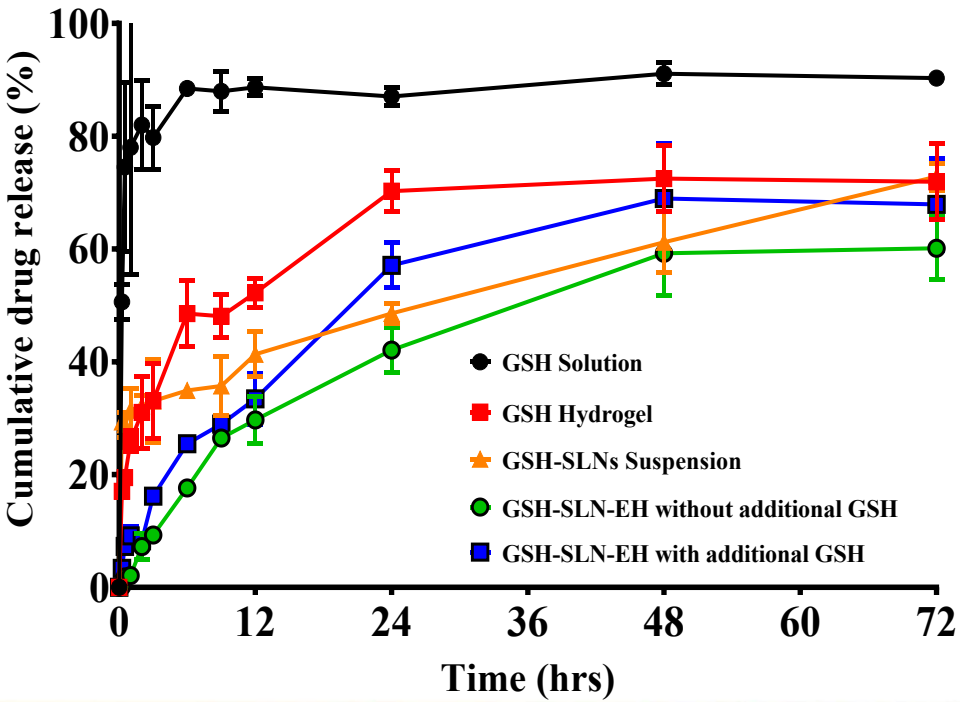
| Chemical | Conditions | Initial | 1 month | 2 months | 3 months |
|---|---|---|---|---|---|
| GSH solution drug content | 4°C | 100% | 68.1 ± 3.6% | 49.2 ± 2.4% | 29.9 ± 2.9% |
| | 25°C | | 62.2 ± 1.8% | 40.1 ± 2.2% | 25.1 ± 2.3% |
| | 40°C | | 51.3 ± 1.7% | 29.1 ± 1.2% | 14.2 ± 1.9% |
| GSH-SLNs drug content | 4°C | 100% | 95.9 ± 2.7% | 92.9 ± 3.1% | 86.1 ± 3.8% |
| | 25°C | | 96.2 ± 1.8% | 90.5 ± 3.6% | 81.5 ± 4.6% |
| | 40°C | | 90.1 ± 2.1% | 85.2 ± 2.8% | 79.2 ± 4.1% |

| Physical | Conditions | Initial | 1 month | 2 months | 3 months |
|---|---|---|---|---|---|
| Particle size (nm) | 4°C | 305.0 ± 0.6 | 315.0 ± 30.6 | 321.5 ± 42.5 | 381.1 ± 41.8 |
| | 25°C | | 334.3 ± 42.2 | 335.9 ± 49.1 | 419.5 ± 107.6 |
| | 40°C | | 415.9 ± 82.6 | 469.7 ± 178.9 | 658.9 ± 188.6 |
| Zeta potential (mV) | 4°C | 20.1 ± 9.5 | 17.1 ± 5.5 | 18.2 ± 8.6 | 15.3 ± 8.1 |
| | 25°C | | 21.9 ± 2.5 | 14.1 ± 8.4 | 10.9 ± 10.4 |
| | 40°C | | 9.5 ± 9.7 | 8.1 ± 9.3 | 4.2 ± 9.2 |

# Stability studies

| Items | Conditions | Initial | 1 month | 2 months | 3 months |
|---|---|---|---|---|---|
| Strength (g) | 4℃ | 5.1 ± 0.5 | 5.2 ± 0.9 | 5.1 ± 1.7 | 5.2 ± 0.9 |
| | 25℃ | | 4.9 ± 1.8 | 4.9 ± 1.1 | 5.2 ± 0.9 |
| | 40℃ | | 6.5 ± 2.9 | 7.2 ± 2.8 | 5.2 ± 0.9 |
| Spreadability (g) | 4℃ | 33.6 ± 1.9 | 34.8 ± 2.5 | 35.7 ± 4.9 | 38.1 ± 5.9 |
| | 25℃ | | 34.6 ± 3.9 | 32.9 ± 3.9 | 38.9 ± 3.8 |
| | 40℃ | | 40.8 ± 5.9 | 42.7 ± 3.4 | 48.9 ± 5.4 |
| Extrudability (g) | 4℃ | 35.9 ± 3.2 | 34.6 ± 2.3 | 35.9 ± 2.5 | 35.6 ± 2.9 |
| | 25℃ | | 35.6 ± 2.7 | 36.7 ± 3.2 | 37.9 ± 3.1 |
| | 40℃ | | 43.7 ± 5.6 | 48.2 ± 6.4 | 52.2 ± 56.4 |
| Thixotropic behaviours | 4℃ | Thixotropic | Thixotropic | Thixotropic | Thixotropic |
| | 25℃ | | Thixotropic | Thixotropic | Thixotropic |
| | 40℃ | | Thixotropic | Thixotropic | Anti-thixotropic |
| Viscoelasticity | 4℃ | Elastic (solid like) | Elastic | Elastic | Elastic |
| | 25℃ | | Elastic | Elastic | Elastic |
| | 40℃ | | Elastic | Viscos | Viscos |

# Drug release




| Samples | Zero order | | First order | | Higuchi | | Korsmeyer-Peppas | | |
|---|---|---|---|---|---|---|---|---|---|
| | $R^2$ | $k_0$ | $R^2$ | $k_1$ | $R^2$ | $k_k$ | $R^2$ | n | $k_h$ |
| GSH-gel | 0.613 | 0.812 | 0.729 | 0.007 | 0.848 | 8.168 | 0.974 * | 0.29 | 1.407 |
| GSH-SLNs | 0.755 | 0.689 | 0.908* | 0.908 | 0.832 | 6.276 | 0.856 | 0.15 | 1.485 |
| EH | 0.844 | 0.901 | 0.908 | 0.006 | 0.971 * | 8.255 | 0.884 | 0.97 | 0.320 |
| EH&GSH | 0.811 | 0.987 | 0.878 | 0.007 | 0.964 | 9.151 | 0.965 * | 0.54 | 0.926 |