LipoMicel: The Science behind the Technology

Julia Solnier, Ph.D.

Director, Medical & Scientific Affairs

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Documentation ✓ Lab Tested ✓

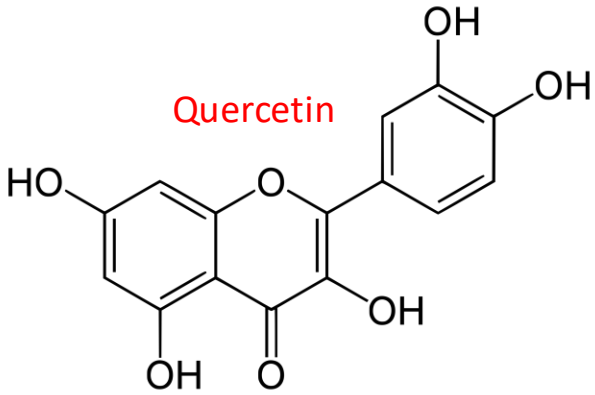
What is Bioavailability?

In nutritional science: "*the fraction (%) of the ingested dose that is absorbed*"

- Many natural compounds are poorly absorbed

➢ due to intestinal endothelium absorption and first-pass metabolism

- great variability between individuals in terms of absorbing nutrients



3,3',4',5,7-Pentahydroxyflavone

$C_{15}H_{10}O_7$

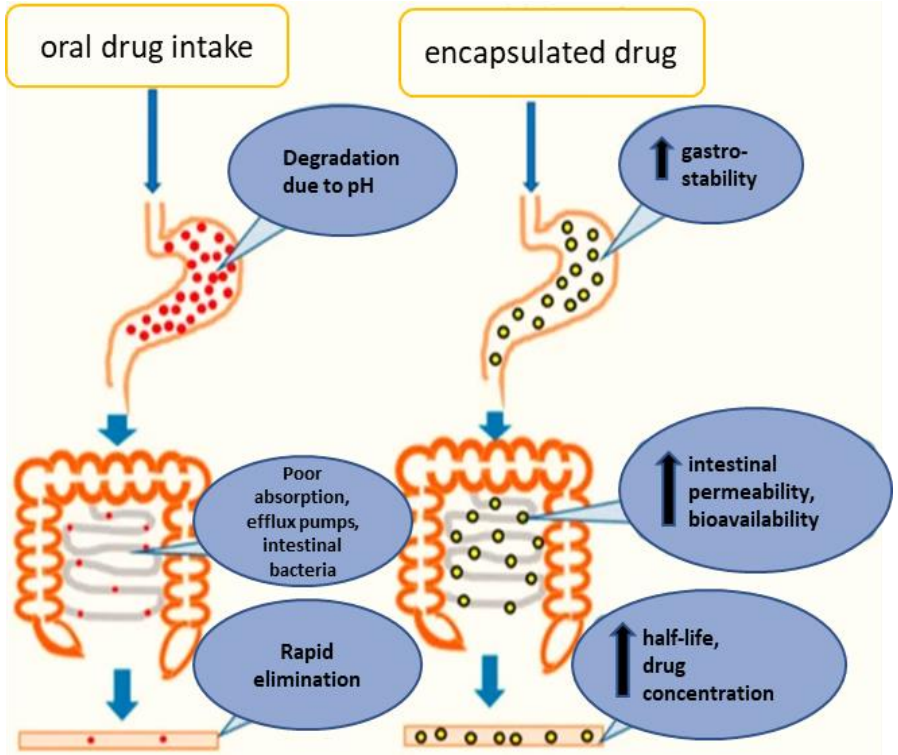
M= 302.236 g/mol

Sophora japonica -> isolated compound

Factors affecting Bioavailability:

- Physical properties of the substance:
  - solubility, molecular size
  - formulation *(delivery system, liquid, powder, or solid)*
  - interactions with foods (administered in a *fed* or *fasted state)*

- Individual differences:
  - Age, ethnicity, gender
  - Diet (e.g., microbiome/gut bacteria)
  - Genetic variations (e.g., metabolic and enzymatic differences)
  - Health status (e.g., gastrointestinal conditions, hepatic or renal dysfunction)
  - Use and interaction with drugs (e.g., antacids, alcohol, nicotine)



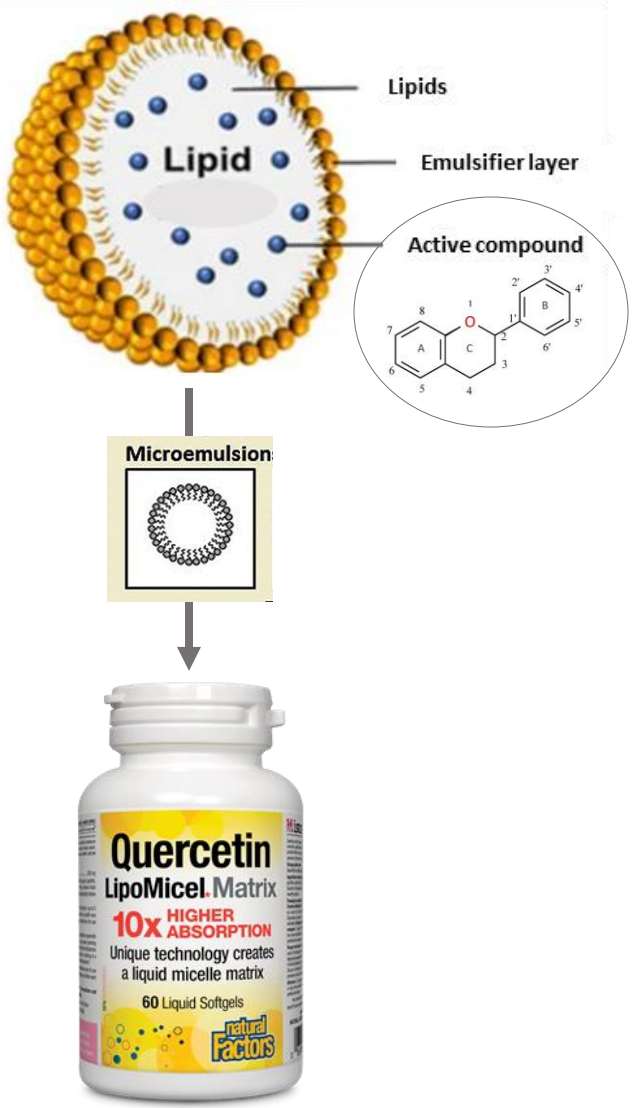
Delivery systems

- a carrier for bioactive compound(s) to cross cell membranes and improve cell uptake

➢ requires both *water & fat solubility + small molecular size*

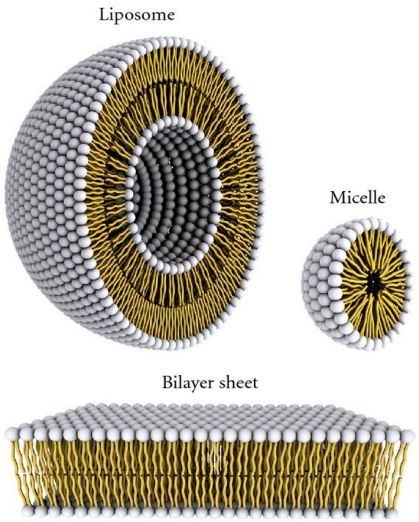
Advantages of Encapsulation:

- small molecular size (micro- or nanometer)
- improved solubility & stability (pH sensitivity): no early degradation in the stomach
- protection against extensive metabolism (gut bacteria, enzymes, etc...)
- prolonged half-life
- lower dose & side effects



LipoMicel vs LipoSomes

- amphiphilic molecules:
- ➢ hydrophilic "water-loving" & hydrophobic "water-repelling" components



https://doi.org/10.5402/2012/738432

Micelles:

- composed of *monolayer* of amphipathic molecules:
- ➢ inner core hydrophobic; hydrophilic outer layers
- formed by aggregation of surfactant molecules (detergents, emulsifiers..)
- smaller size than liposomes

Liposomes:

- composed of *bilayer* of amphipathic molecules:
- ➢ inner core hydrophilic; hydrophobic bilayers
- formed by phospholipid molecules (e.g., lecithin), and cholesterol

In-vitro Research

1. Solubility studies:

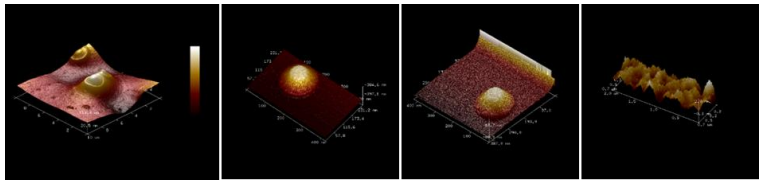
- in gastric and intestinal media: mimicking the pH environment in the human body
- predictor of absorption and bioavailability

2. Caco-2-cell studies:

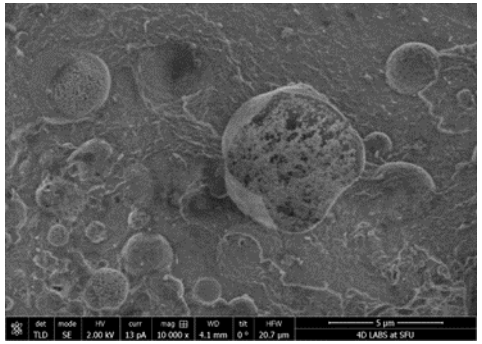
- a cell line derived from human colon carcinoma
- similar characteristics to cells lining the small intestine
- used for permeability, absorption, interactions, toxicity & safety studies

3. Characterization of the LipoMicel particles:

- particle size distribution: Dynamic Light Scattering (DLS)
- stability: Zeta potential
- morphology, size, and shape: Scanning Electron Microscopy (SEM)



Atomic force microscopy quercetin in LM in 3-D representation



Cryo-SEM shows berberine present inside the micelles of LM

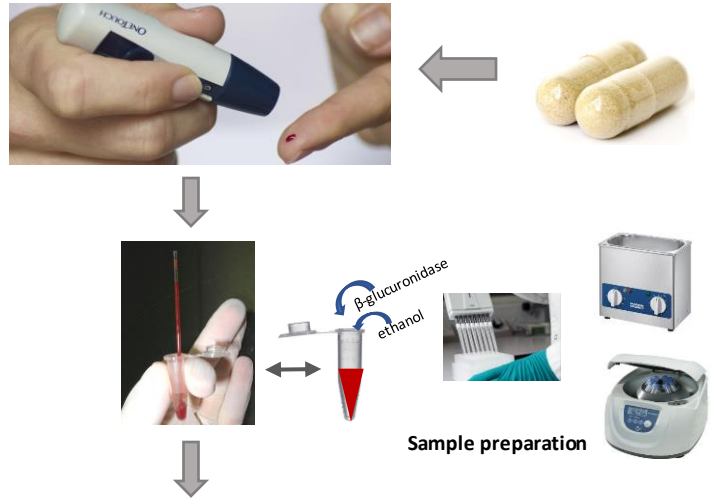
Clinical Research

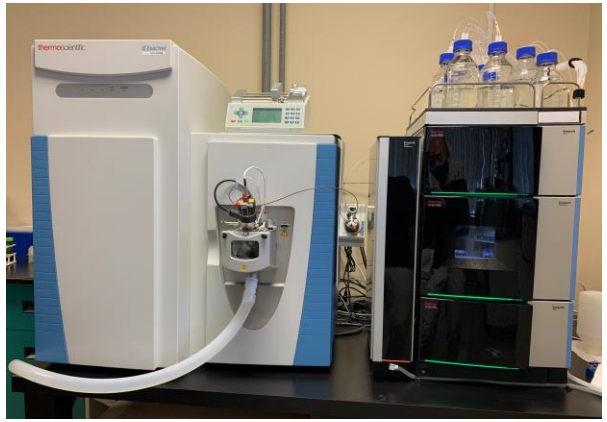
1. Bioavailability studies in humans:

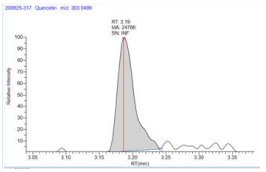
- to measure the absorption of a compound in LipoMicel formulation
- to compare it with standard (unformulated) product + competitor formulations

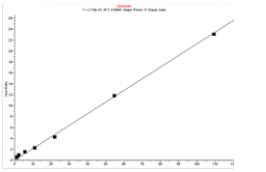
- Methods:

- Crossover studies with 10-15 participants
- Treatments administered in *fasted* or *fed* state
- Collection of capillary blood samples at intervals from 0-24hrs or longer
- high-resolution analyzer: UHPLC coupled to Orbitrap Mass Spectrometer





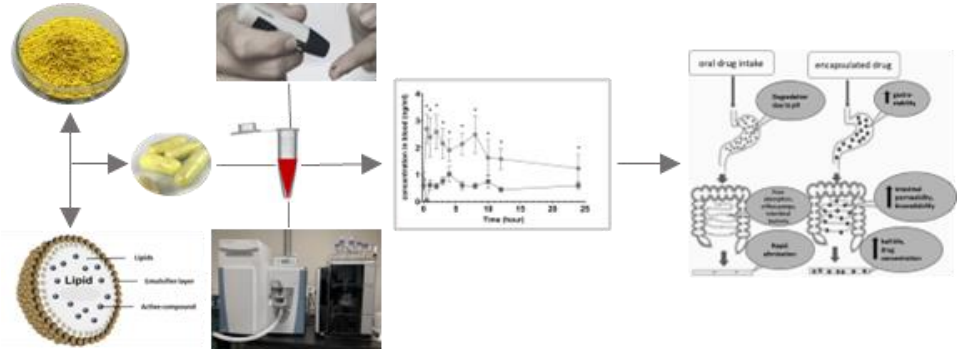




Clinical Research

2. Safety studies in humans:

- to monitor adverse events or side effects of LipoMicel formulations
- Surveys/health questionnaires as well as blood collections over 2 or 4 weeks



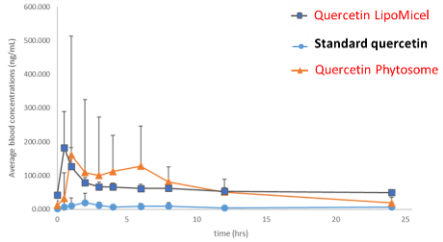
- Methods*:*

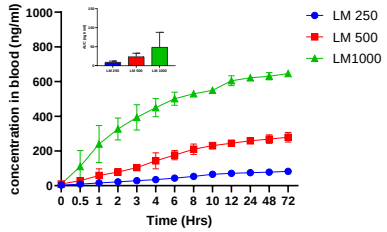
- Placebo-controlled, parallel study design
- Collection of capillary and/or venous blood samples
- Clinical chemistry: alanine aminotransferase (ALT), aspartate transaminase (AST), total bilirubin, creatinine, electrolytes (Na, K, Cl), & estimated glomerular filtration rate (eGFR)

Results

1. Quercetin LipoMicel

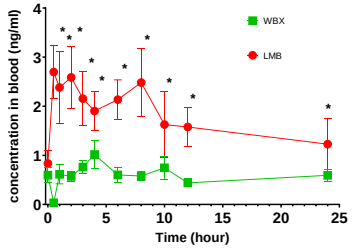
- 10-fold higher concentrations of LipoMicel (LM) vs standard
- Accumulating concentrations over 72hrs, at doses 250 mg, 500 mg, or 1,000 mg

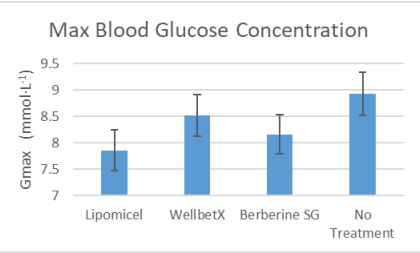




2. Berberine LipoMicel

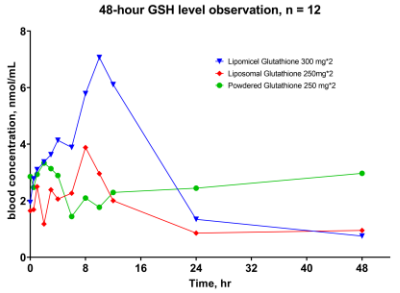
- 3-fold higher concentrations of LM vs standard
- Higher gastrointestinal solubility (20-34-fold) and cell permeability
- effective in lowering blood glucose levels by 12% in as short as 2 days

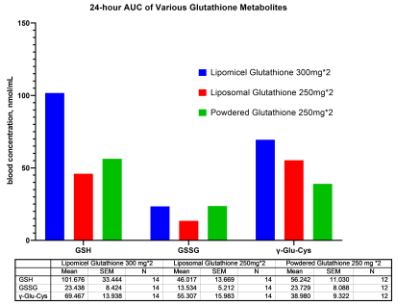




3. Glutathione LipoMicel

- 2-fold higher concentrations of LM vs Liposomal and standard
- Approx. 2-fold higher metabolite concentrations γ-glutamylcysteine (γ-GC)





Results on Safety

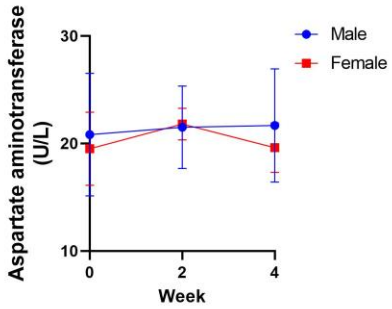
- No record of any adverse events and side effects during the 24-hr and 72-hr study periods.

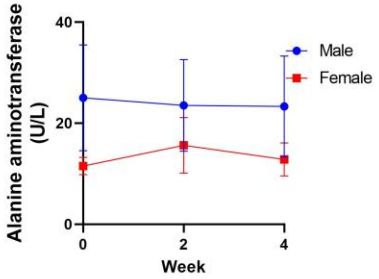
1. Berberine LipoMicel

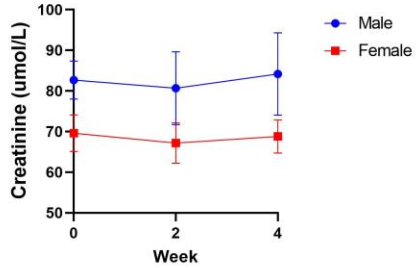
- No significant changes in safety blood markers over a period of 30-days
- No or mild gastrointestinal side effects after taking berberine for 30-days

2. Glutathione LipoMicel

- No significant changes in safety blood markers over a period of 30-days
- Mild gastrointestinal side effects after taking glutathione for 30-days







Research papers on LipoMicel products

Journal of Natural Health Product Research
2021, Vol. 3, Iss. 2, pp. 1–8.
NHPPublications.com

Journal of Natural Health Product Research
NHP PUBLICATIONS

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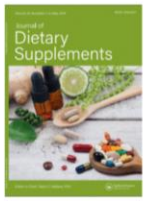
ORIGINAL RESEARCH OPEN ACCESS

Quercetin LipoMicel—A Novel Delivery System to Enhance Bioavailability of Quercetin

Julia Solnier, PhD[1,*], Chuck Chang, BSc[1], Kyle Roh, BSc[1], Min Du, MSc[1], Yun Chai Kuo, BEng[1], Mary Hardy, MD[2], Michael Lyon, MD[3,4], Roland Gahler[5]

[1]ISURA, Burnaby, BC, Canada
[2]Association of Integrative and Holistic Medicine, San Diego, California, USA
[3]Obesity Medicine and Diabetes Institute, Coquitlam, BC, Canada
[4]Department of Family Practice, Faculty of Medicine, University of British Columbia, Vancouver, BC, Canada
[5]Factors Group of Nutritional Products Inc. R&D, Burnaby, BC, Canada
*Corresponding Author: jsolnier@factorsgroup.com



Pharmacokinetics of different Quercetin formulations in healthy volunteers: a diet-controlled, crossover, single- and multiple dose plasma uptake study

Journal:	*Journal of Dietary Supplements*
Manuscript ID	WJDS-2022-0116.R1
Manuscript Type:	Original Research Article
Date Submitted by the Author:	27-Jun-2022
Complete List of Authors:	Solnier, Julia; ISURA, Clinical Research Zhang, Yiming ; ISURA, Clinical Research Roh, Kyle; ISURA, Clinical Research Kuo, Yun; ISURA, Clinical Research Wood, Simon; University of British Columbia, Food, Nutrition and Health Program, Faculty of Land and Food Systems Gahler, Roland; Factors Group , R & D Chang, Chuck; ISURA, Clinical Research
Keywords:	Flavonoid, food-grade delivery system, Quercetin, Quercetin LipoMicel, Human Studies, Antioxidant, bioavailability, plasma uptake

Journal of Natural Health Product Research
NHP PUBLICATIONS

A pilot crossover study of Berberine and its Short-term Effects on Blood Glucose Levels in healthy volunteers

Chuck Chang, BSc [1], Kyle Roh, BSc [1], Min Du, MSc [1], Yun Chai Kuo, BSc [1], Yiming Zhang, Ph.D. [1] Mary Hardy, MD [2], Roland Gahler [3], Julia Solnier, Ph.D. [1] *

[1] ISURA, Burnaby, BC, Canada, V3N 4T5
[2] Association of Integrative and Holistic Medicine, San Diego, California, USA.
[3] Natural Factors Nutritional Products Ltd, Coquitlam, BC, Canada V3K 6Y2

*Corresponding Author: jsolnier@isura.ca

ScienceDirect

Current Research in Pharmacology and Drug Discovery

A characterization and plasma uptake study: A new Berberine formulation with enhanced absorption in vitro and in healthy volunteers

--Manuscript Draft--

Manuscript Number:	CRPHAR-D-23-00052
Full Title:	A characterization and plasma uptake study: A new Berberine formulation with enhanced absorption in vitro and in healthy volunteers
Article Type:	Research Paper
Corresponding Author:	Julia Solnier, Ph.D ISURA Burnaby, British Columbia CANADA
Corresponding Author's Institution:	ISURA
Other Authors:	Yiming Zhang, Ph.D
	Yun Chai Kuo, B.Sc.
	Min Du, M.Sc.
	Kyle Roh, M.Sc.
	Mary Hardy, M.D
	Simon Wood, Ph.D
	Roland Gahler
	Chuck Chang, B.Sc.
First Author:	Julia Solnier, Ph.D

ORIGINAL RESEARCH

A Randomized, Double-blind, Crossover, Pharmacokinetics study and a 30-day Safety Evaluation of Micellar Glutathione in healthy participants

Julia Solnier[1] *, Yiming Zhang[1], Kyle Roh[1], Yun Chai Kuo[1], Mary Hardy[5], Roland J Gahler[6], Chuck Chang[1]

[1]ISURA, Burnaby, BC V3N4S9, Canada; jsolnier@isura.ca; yzhang@isura.ca, kroh@isura.ca, rkuo@isura.ca, cchang@isura.ca

[2]School of Public Health, Faculty of Health Sciences, Curtin University, Perth, WA 6845, Australia; simonwood@shaw.ca

[3]InovoBiologic Inc., Calgary, AB Y2N4Y7, Canada; simonwood@shaw.ca

[5]Association of Integrative and Holistic Medicine, San Diego, California, USA mary@maryhardy.com

[6]Factors Group R & D, Burnaby, BC V3N4S9, Canada; rgahler@factorsgroup.com

nutraceuticals MDPI

Article

Designing Vitamin D_3 Formulations: An In Vitro Investigation Using a Novel Micellar Delivery System

Min Du [1], Chuck Chang [1], Xin Zhang [2], Yiming Zhang [1], Melissa J. Radford [3], Roland J. Gahler [4], Yun Chai Kuo [1], Simon Wood [5,6,7] and Julia Solnier [1,*]

[1] ISURA, Burnaby, BC V3N4S9, Canada; mdu@isura.ca (M.D.); cchang@isura.ca (C.C.); yzhang@isura.ca (Y.Z.); rkuo@isura.ca (Y.C.K.)
[2] 4D LABS, Simon Fraser University, 8888 University Drive, Burnaby, BC V5A 1S6, Canada; xinz@sfu.ca
[3] Department of Chemistry and 4D LABS, Simon Fraser University, 8888 University Drive, Burnaby, BC V5A 1S6, Canada; melissa_radford@sfu.ca
[4] Factors Group R & D, Burnaby, BC V3N4S9, Canada; rgahler@factorsgroup.com
[5] School of Public Health, Faculty of Health Sciences, Curtin University, Perth, WA 6845, Australia; simonwood@shaw.ca
[6] InovoBiologic Inc., Calgary, AB Y2N4Y7, Canada
[7] Food, Nutrition and Health Program, University of British Columbia, Vancouver, BC V6T1Z4, Canada
* Correspondence: jsolnier@isura.ca

Abstract: Vitamin D is an essential nutrient with important immunomodulatory properties. As a fat-soluble compound, Vitamin D (and its D_3 form) is immiscible with water, which presents challenges to absorption. In an in vitro setting, the current study characterizes novel micellar formulations of Vitamin D_3 designed to improve absorption. Techniques used to evaluate and compare the micellar formulations against a non-micellar formula include the following: cryo-SEM to determine morphology; laser diffraction to determine particle size and distribution; zeta potential to determine stability of the particles; solubility assays to determine solubility in water and gastrointestinal media; and Caco-2 cell monolayers to determine intestinal permeability. Results show advantageous features (particle size range in the low micrometres with an average zeta potential of -51.56 ± 2.76 mV), as well as significant improvements in intestinal permeability, in one optimized micellar formula (LipoMicel®). When introduced to Caco-2 cells, LipoMicel's permeability was significantly better than the control ($p < 0.01$; ANOVA). Findings of this study suggest that the novel micellar form of Vitamin D_3 (LipoMicel) has the potential to promote absorption of Vitamin D_3. Thus, it can serve as a promising candidate for follow-up in vivo studies in humans.

Keywords: Vitamin D; cholecalciferol; bioavailability; Caco-2 cell-permeability; delivery systems; electron microscopy; cryo-SEM; laser diffraction; zeta potential

check for updates

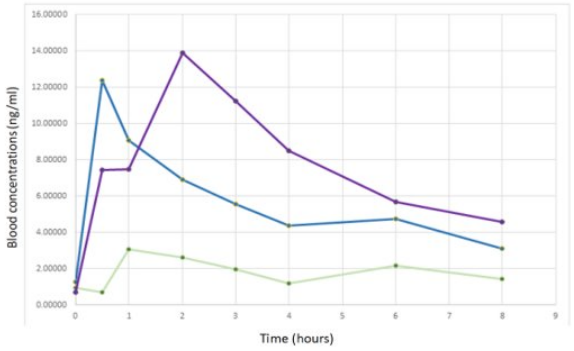
Citation: Du, M.; Chang, C.; Zhang, X.; Zhang, Y.; Radford, M.J.; Gahler, R.J.; Kuo, Y.C.; Wood, S.; Solnier, J. Designing Vitamin D_3 Formulations: An In Vitro Investigation Using a Novel Micellar Delivery System. *Nutraceuticals* **2023**, *3*, 290–305. https://doi.org/10.3390/nutraceuticals3020023

Frequent Questions

- **Lipomicel** Quercetin vs **EMIQ**?
- **Micelles** vs **liposomes**—which formulation works best?

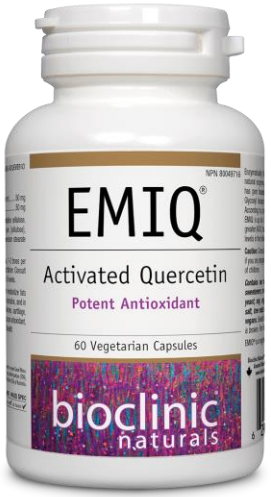
➢ Fat-soluble vs water-soluble compounds (like Vit C)

- Soft gels vs liquids (in liposomal form)



500mg of each preparation was given to each volunteer; average data presented

500 mg LipoMicel Quercetin (2 softgels)
500 mg Bioactive Quercetin EMIQ (10 capsules)
500mg Standard Quercetin (1 capsule)



Thank you very much for your attention!

Study references:

- Solnier et al. (2021) Quercetin LipoMicel—A Novel Delivery System to Enhance Bioavailability of Quercetin: https://doi.org/10.33211/jnhpr.17
- Solnier et al. (2023) Pharmacokinetics of different Quercetin formulations in healthy volunteers: a diet-controlled, crossover, single- and multiple dose plasma uptake study (paper in revision)
- Solnier et al. (2023) A characterization and plasma uptake study: A new Berberine formulation with enhanced absorption in vitro and in healthy volunteers (paper in review)
- Chang et al. (2023) A pilot crossover study of Berberine and its Short-term Effects on Blood Glucose Levels in healthy volunteers (paper accepted for publication).
- Solnier et al. (2023) A Randomized, Double-blind, Crossover, Pharmacokinetics study and a 30-day Safety Evaluation of Micellar Glutathione in healthy participants (paper in preparation).
- Du et al. (2023) Designing Vitamin D3 Formulations: An In Vitro Investigation Using a Novel Micellar Delivery System: https://doi.org/10.3390/nutraceuticals3020023