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TECNOLOGIAS PARA MELHORAR A ABSORÇÃO DOS SUPLEMENTOS

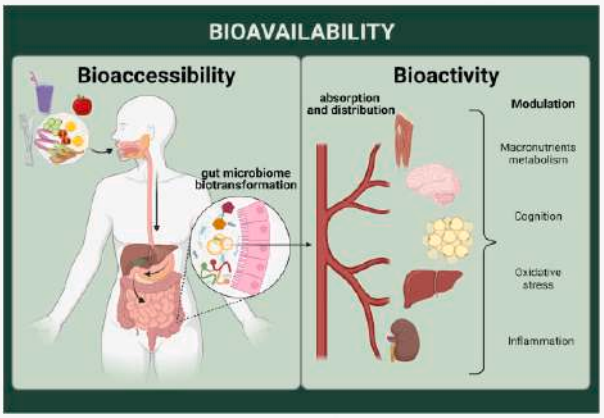
Prof. Márcio Souza

Doutor e Mestre em Saúde do Adulto pela Faculdade de Medicina da UFMG
Pós-graduado em Nutrição Esportiva Funcional
Pós-graduado em Nutrição Clínica Funcional
Pós-graduado em Fitoterapia Funcional
Pós-graduado em Treinamento Desportivo
Especialista em Fitoterapia pela Asbran
Professor no curso de graduação em Nutrição na Faminas-BH
Professor nos cursos de pós-graduação da VP Centro de Nutrição Funcional
Autor dos livros: "Nutrientes aplicados à prática clínica" e "Suplementação Nutricional: guia prático para o atendimento"

@marcionutricionista **/MarcioNutricionista**

MASTERCLASS
SUPLEMENTAÇÃO EM **GOTAS BIOATIVAS**

BIODISPONIBILIDADE



Defining Bioavailability

Until a nutrient passes from the digestive system into the bloodstream, it has little or no value. Bioavailability can be explained as the amount of a nutrient absorbed from the gut that becomes available for normal physiological functions or storage.

doi: 10.1146/annurev-food-030216-030055
doi: 10.1016/B978-0-12-384947-2.00068-4

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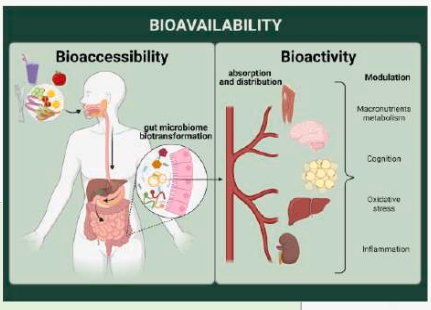
BIODISPONIBILIDADE



S = ***Species*** **(especiação do nutriente)**
L = ***Linkage*** **(ligação molecular)**
A = ***Amount consumed in a meal*** **(qtde consumida na refeição)**
M = ***Matrix in wich the nutrient is incorporated*** **(matriz onde o nutriente é incorporado)**
A = ***Attenuators of absorption and bioconversion*** **(atenuantes da absorção e bioconversão)**
N = ***Nutrient status of the host*** **(estado nutricional do hospedeiro)**
G = ***Genetic factors*** **(fatores genéticos)**
H = ***Host related factors*** **(fatores relacionados com o hospedeiro)**
I = ***Interaction*** **(interações)**

Cozzolino SMF. Biodisponibilidade de nutrientes. 6ª ed. 2021

BIODISPONIBILIDADE

NUTRIENTE COM BIODISPONIBILIDADE BAIXA → PROBLEMA PARA O PRESCRITOR

SOLUÇÃO PARA O PROBLEMA → TECNOLOGIAS

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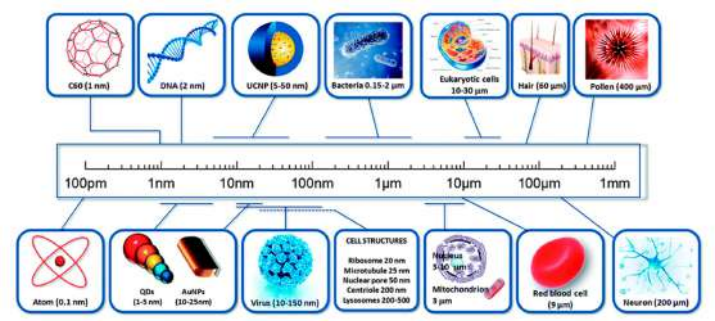
NANOTECNOLOGIA

The History of Nanoscience and Nanotechnology: From Chemical–Physical Applications to Nanomedicine



Molecules; 25(1):112, Dec 2019
doi: 10.3390/molecules25010112

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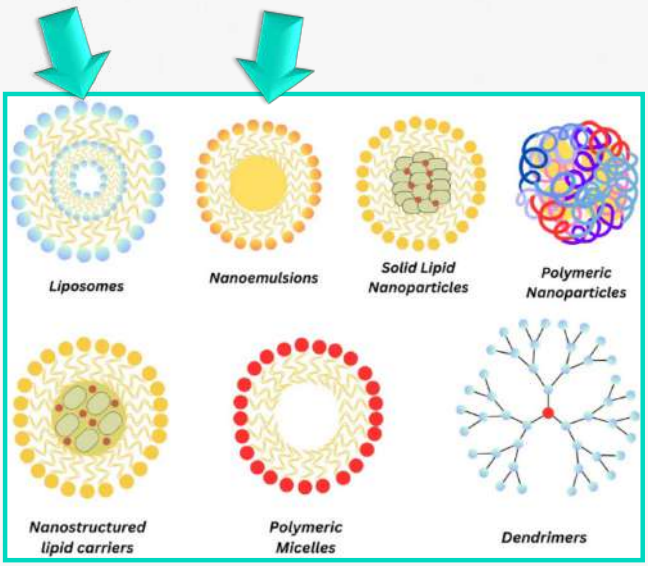
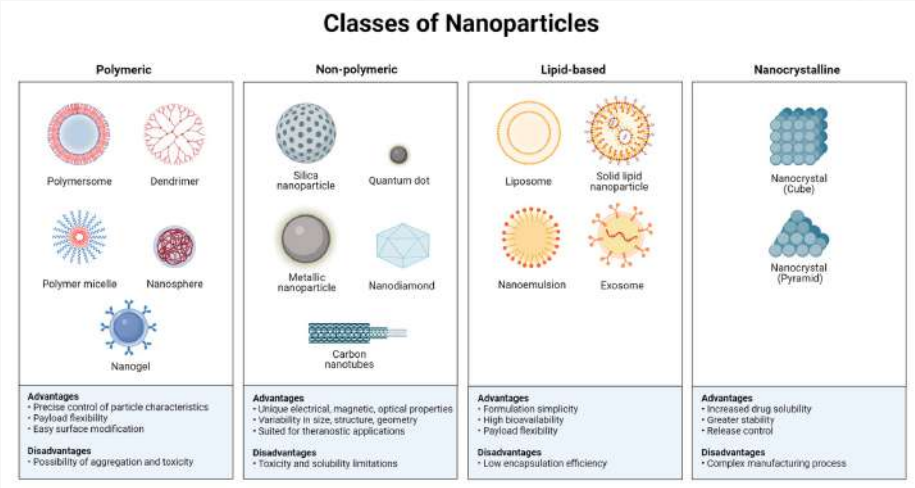


NANOCARREADORES

Nanomaterials (Basel); 14(8):672, 2024
doi: 10.3390/nano14080672

NANOCARREADORES

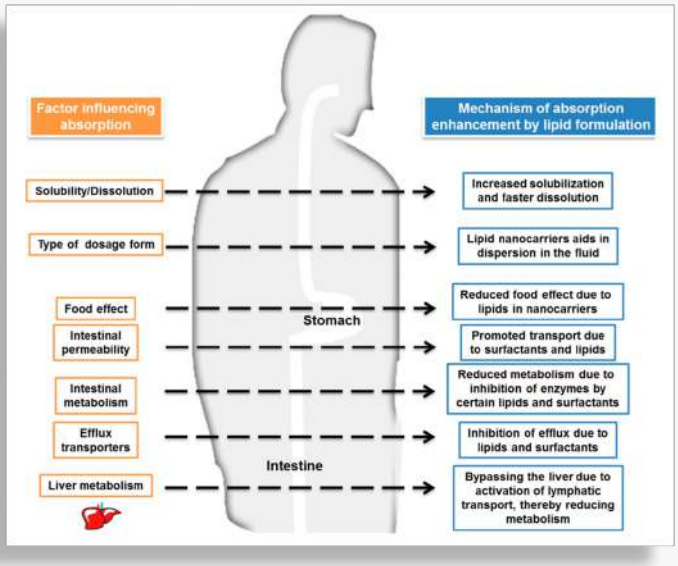
Application of Nanoparticles in Human Nutrition: A Review



Nutrients; 16(5):636, 2024
doi: 10.3390/nu16050636

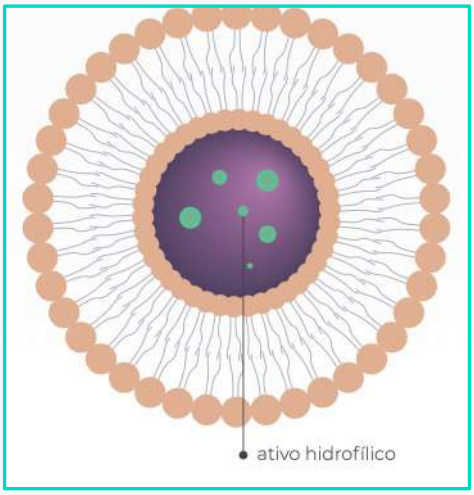
NANOCARREADORES LIPÍDICOS

Use of Lipid Nanocarriers to Improve Oral Delivery of Vitamins



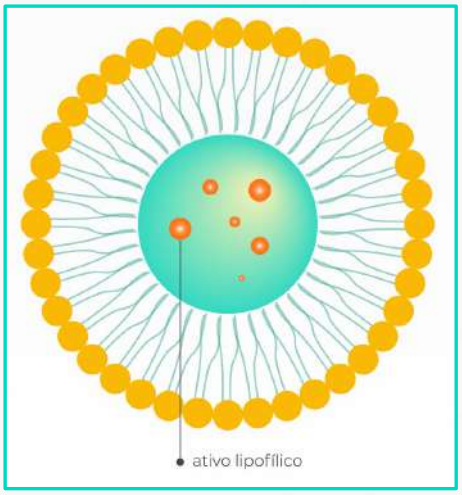
Nutrients; 11(1):68, 2019
doi: 10.3390/nu11010068

LIPOSSOMAL



Ex: B12, Melatonina...

NANOEMULSÃO



Ex: CoQ10...

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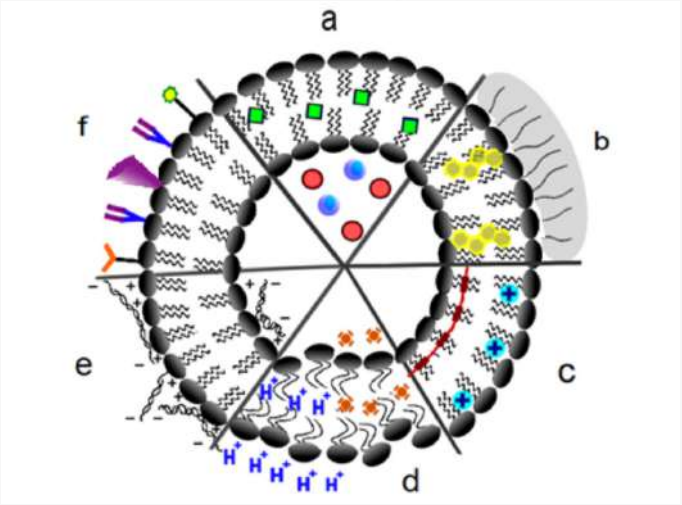
LIPOSSOMAL

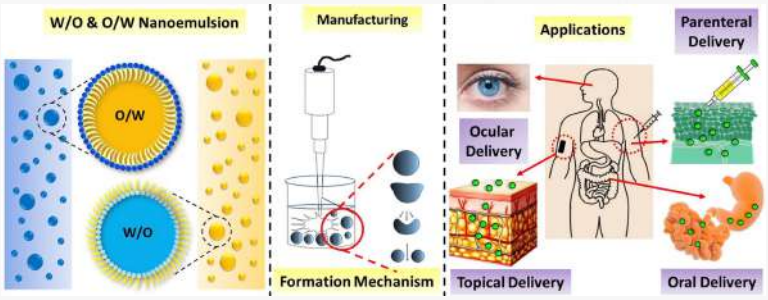
Liposomal Drug Delivery: A Versatile Platform for Challenging Clinical Applications



J Pharm Pharm Sci; 17(3):401-26, 2014
doi: 10.18433/j3cp55

NANOEMULSÃO

Nanoemulsion: Concepts, development and applications in drug delivery



J Control Release; 252:28-49, 2017
doi: 10.1016/j.jconrel.2017.03.008

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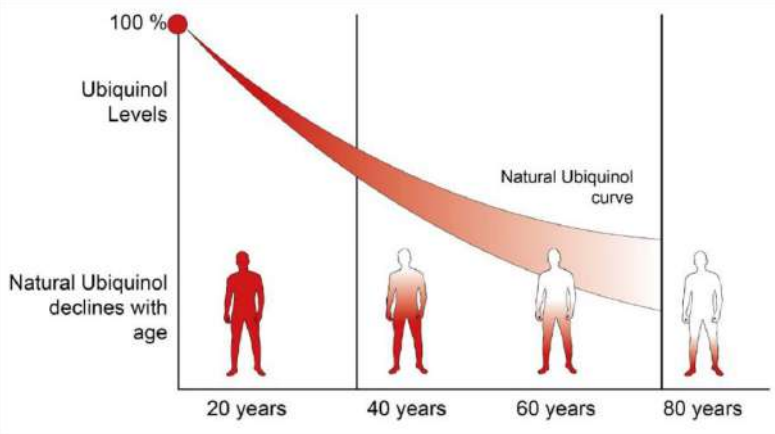
COENZIMA Q10

COENZIMA Q10



PRODUÇÃO ENDÓGENA

Nutrients; 14(20):4326, 2022
doi: 10.3390/nu14204326

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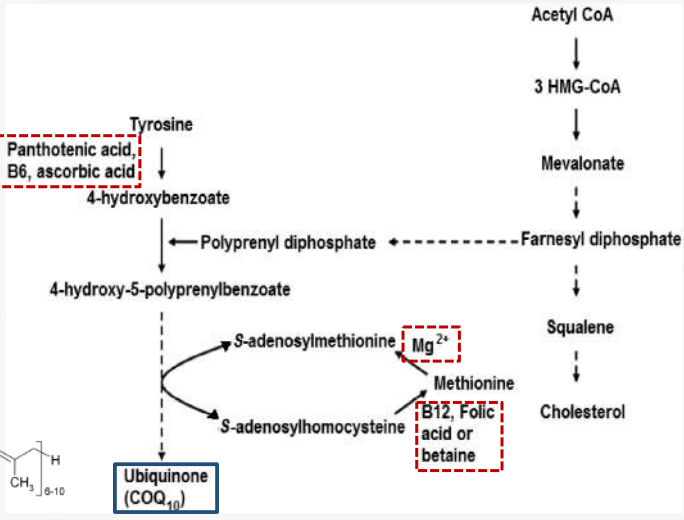
COENZIMA Q10



COENZIMA Q10

INTERAÇÕES & BIODISPONIBILIDADE

Drogas como as estatinas (inibidores da HMG-CoA redutase), beta-bloqueadores, hidroclorotiazida, metildopa e antidepressivos tricíclicos podem depletar Q10

SOUZA, MLR. Suplementação nutricional: guia prático para o atendimento (2021)

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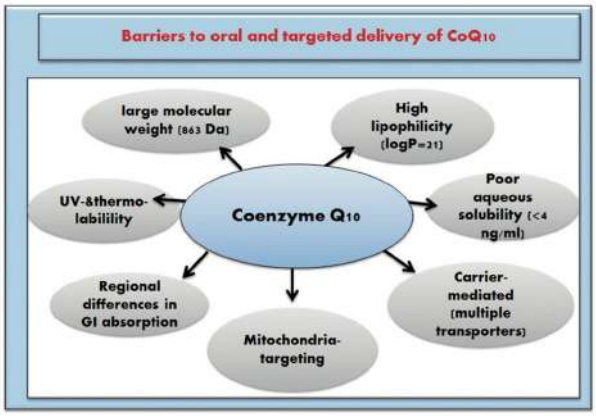
Strategies for oral delivery and mitochondrial targeting of CoQ10



Biodisponibilidade da CoQ10

- Instável em exposição ao ar, luz UV e temperaturas altas
- Alto peso molecular
- Altamente lipofílica e baixa solubilidade em água
- Depende de múltiplos transportadores
- Diferenças na absorção no TGI em diferentes regiões

Drug Deliv; 23(6):1868-81, 2016
doi: 10.3109/10717544.2014.993747

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Biodisponibilidade da CoQ10

Coenzyme Q10 supplementation: Efficacy, safety, and formulation challenges

Highlights
- Third most consumed nutritional supplement
- Essential role in mitochondrial bioenergetics and oxidative stress
- Higher levels in tissues with high metabolic activity
- Candidate for the treatment of various diseases
- Highly safe
- Synthesized from tyrosine
- Different factors can lower its concentration

Pharmacokinetics
- Slow and incomplete absorption (Tmax: 6h)
- Low bioavailability

Physicochemical properties
- Yellow to orange
- Crystalline powder
- Fine particle size
- Tasteless with slight odour
- Lipophilic
- High molecular weight
- Melting point: 48ºC

COENZYME Q10
UBIQUINONE

Solubility
- Insoluble in water
- Slightly soluble in ethanol
- Soluble in acetone and ether

Stability
- Vulnerable to heat, light and oxygen
- Stored in a dry place, protected from light and below 25ºC. Stable for 24 months.

Formulation challenges
- Solubility
- Stability
- Bioavailability
- Rheology
- Low melting point

Compr Rev Food Sci Food Saf; 19(2):574-594, 2020
doi: 10.1111/1541-4337.12539

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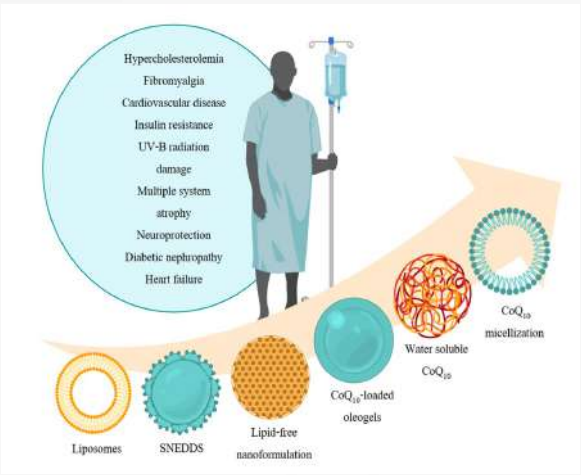
COENZIMA Q10

Coenzyme Q_{10}: Novel Formulations and Medical Trends

Abstract: The aim of this review is to shed light over the most recent advances in Coenzyme Q_{10} (CoQ_{10}) applications as well as to provide detailed information about the functions of this versatile molecule, which have proven to be of great interest in the medical field. Traditionally, CoQ_{10} clinical use was based on its antioxidant properties; however, a wide range of highly interesting alternative functions have recently been discovered. In this line, CoQ_{10} has shown pain-alleviating properties in fibromyalgia patients, a membrane-stabilizing function, immune system enhancing ability, or a fundamental role for insulin sensitivity, apart from potentially beneficial properties for familial hypercholesterolemia patients. In brief, it shows a remarkable amount of functions in addition to those yet to be discovered. Despite its multiple therapeutic applications, CoQ_{10} is not commonly prescribed as a drug because of its low oral bioavailability, which compromises its efficacy. Hence, several formulations have been developed to face such inconvenience. These were initially designed as lipid nanoparticles for CoQ_{10} encapsulation and distribution through biological membranes and eventually evolved towards chemical modifications of the molecule to decrease its hydrophobicity. Some of the most promising formulations will also be discussed in this review.



Int J Mol Sci; 21(22):8432, 2020
doi: 10.3390/ijms21228432

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Bioavailability of coenzyme Q10 supplements depends on carrier lipids and solubilization

Objectives: Bioavailability of supplements with coenzyme Q10 (CoQ_{10}) in humans seems to depend on the excipients of formulations and on physiological characteristics of the individuals. The aim of this study was to determine which factors presented in CoQ_{10} supplements affect the different response to CoQ_{10} in humans.

Methods: We tested seven different supplement formulations containing 100 mg of CoQ_{10} in 14 young, healthy individuals. Bioavailability was measured as area under the curve of plasma CoQ_{10} levels over 48 h after ingestion of a single dose. Measurements were repeated in the same group of 14 volunteers in a double-blind crossover design with a minimum of 4 wk washout between intakes.

Results: Bioavailability of the formulations showed large differences that were statistically significant. The two best absorbable formulations were soft-gel capsules containing ubiquinone (oxidized CoQ_{10}) or ubiquinol (reduced CoQ_{10}). The matrix used to dissolve CoQ_{10} and the proportion and addition of preservatives such as vitamin C affected the bioavailability of CoQ_{10}. Although control measurements documented that all formulations contained 100 mg of either CoQ_{10} or ubiquinol, some of the participants showed high and others lower capacity to reach high increase of CoQ_{10} in blood, indicating the participation of individual unknown physiological factors.

Conclusion: This study highlights the importance of individually adapted selection of best formulations to reach the highest bioavailability of CoQ_{10} in humans.

COENZIMA Q10

Cada indivíduo responde de um jeito ao uso da CoQ10 tradicional, demonstrando uma capacidade maior ou menor de apresentar aumentos de CoQ10 no sangue.

Esse estudo reforça a importância de individualmente selecionar as melhores formulações para atingir a mais alta biodisponibilidade

A FORMA DE NANOEMULSÃO É UMA EXCELENTE OPÇÃO ATUALMENTE

Nutrition; 57:133-140, 2019
doi: 10.1016/j.nut.2018.05.020

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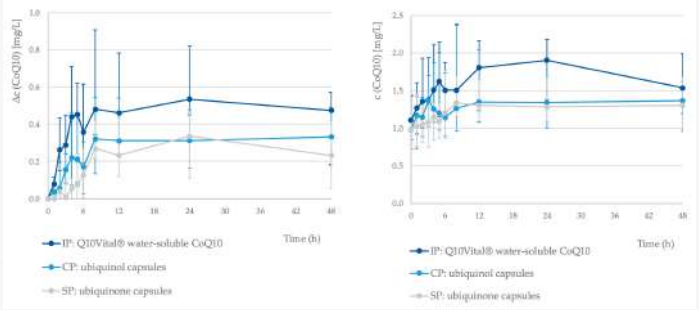
Comparative Bioavailability of Different Coenzyme Q10 Formulations in Healthy Elderly Individuals

Abstract: Coenzyme Q10 (CoQ10) plays a central role in mitochondrial oxidative phosphorylation. Several studies have shown the beneficial effects of dietary CoQ10 supplementation, particularly in relation to cardiovascular health. CoQ10 biosynthesis decreases in the elderly, and consequently, the beneficial effects of dietary supplementation in this population are of greater significance. However, most pharmacokinetic studies have been conducted on younger populations. The aim of this study was to investigate the single-dose bioavailability of different formulations of CoQ10 in a healthy geriatric population. A randomized, three-period, crossover bioavailability study was conducted on 21 healthy older adults (aged 65–74). The treatment was a single dose with a one-week washout period. Three different formulations containing the equivalent of 100 mg of CoQ10 were used: Q10Vital® water-soluble CoQ10 syrup (the investigational product—IP); ubiquinol capsules (the comparative product—CP); and ubiquinone capsules (the standard product—SP). Ubiquinone/ubiquinol was followed in the plasma for 48 h. An analysis of the ratio of the area under the baseline-corrected concentration curve (ΔAUC_{48}) for total CoQ10 and a comparison to SP yielded the following: The bioavailability of CoQ10 in the IP was 2.4-fold higher (95% CI: 1.3–4.5; $p = 0.002$), while the bioavailability of ubiquinol (CP) was not significantly increased (1.7-fold; 95% CI: 0.9–3.1, $p = 0.129$). No differences in the redox status of the absorbed coenzyme Q10 were observed between formulations, showing that CoQ10 appeared in the blood mostly as ubiquinol, even if consumed as ubiquinone.

COENZIMA Q10

Randomizado, cruzado
21 indivíduos saudáveis com idades entre 65 e 74 anos
Dose única com uma semana de washout entre os testes
G1: 100 mg de CoQ10 solúvel em água
G2: 100 mg de CoQ10 em cápsula na forma de ubiquinol
G3: 100 mg de CoQ10 em cápsula na forma de ubiquinona



A biodisponibilidade da CoQ10 hidrossolúvel foi 2,4x mais alta.

Nutrients; 12(3):784, 2020
doi: 10.3390/nu12030784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SUPLEMENTAÇÃO
EM GOTAS BIOATIVAS
BioQ10
TECNOLOGIA YDROSOLV
LANÇAMENTO
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SUPLEMENTAÇÃO
EM GOTAS BIOATIVAS
INFORMAÇÃO NUTRICIONAL
Porções por embalagem: Cerca de 27
Porção: 0,55 ml (10 gotas)
0,55 ml
%VD*
Carboidratos (g) 0,5 0
Coenzima Q10 (mg) 100
Não contém quantidades significativas de valor energético, açúcares totais, açúcares adicionados, proteínas, gorduras totais, gorduras saturadas, gorduras trans, fibras alimentares e sódio.
*Percentual de valores diários fornecidos pela porção.
Ingredientes:
Coenzima Q10, água, triglicerídeos de cadeia média, agente de massa glicerol e emulsificante lecitina.
ALÉRGICOS: CONTÉM DERIVADOS DE SOJA.
LINHA GOTAS®
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VITAMINA B12

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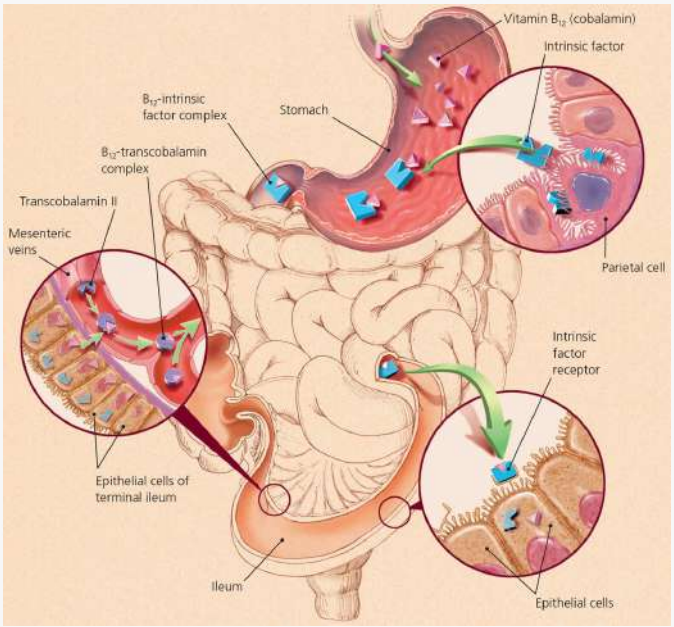

VITAMINA B12

A biodisponibilidade da B12 é altamente dependente do trato gastrointestinal

Fator intrínseco, HCl e íleo terminal

Armazenamento: Fígado (60%) e Músculos (30%)

Público de Risco:
- **Idosos**
- **Vegetarianos e Veganos**
- **Bariátricos**
- **Uso crônico de alguns medicamentos**

SOUZA, MLR. Suplementação nutricional: guia prático para o atendimento (2021)

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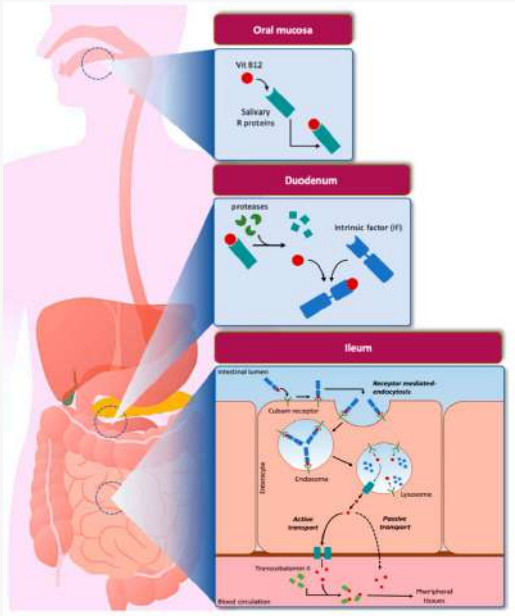
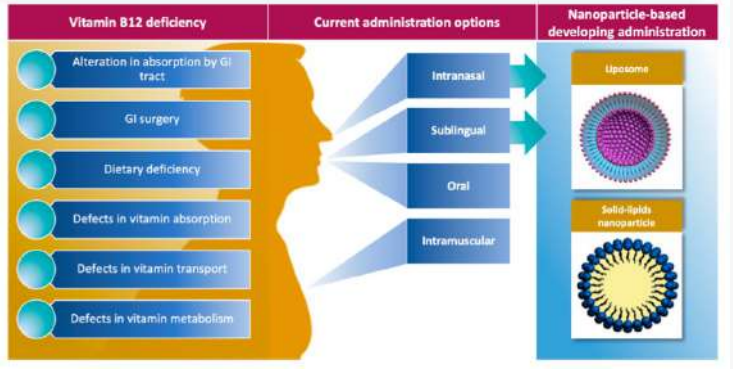
VITAMINA B12



Current Nanocarrier Strategies Improve Vitamin B12 Pharmacokinetics, Ameliorate Patients' Lives, and Reduce Costs



Nanomaterials (Basel); 11(3):743, 2021
doi: 10.3390/nano11030743

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SUPLEMENTAÇÃO EM **GOTAS BIOATIVAS**

INFORMAÇÃO NUTRICIONAL

Porções por embalagem: Cerca de 750
Porção: 0,04 ml (1 gota)

	0,04 ml	%VD* (maiores de 19 anos)	%VD* (gestantes)	%VD* (lactantes)
Vitamina B12 (µg)	9,9	413	381	354

Não contém quantidades significativas de valor energético, carboidratos, açúcares totais, açúcares adicionados, proteínas, gorduras totais, gorduras saturadas, gorduras trans, fibras alimentares e sódio.

*Percentual de valores diários fornecidos pela porção.

Ingredientes:
Água, metilcobalamina, agente de massa glicerol e emulsificante lecitina.
ALÉRGICOS: CONTÉM DERIVADOS DE SOJA.

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MELATONINA

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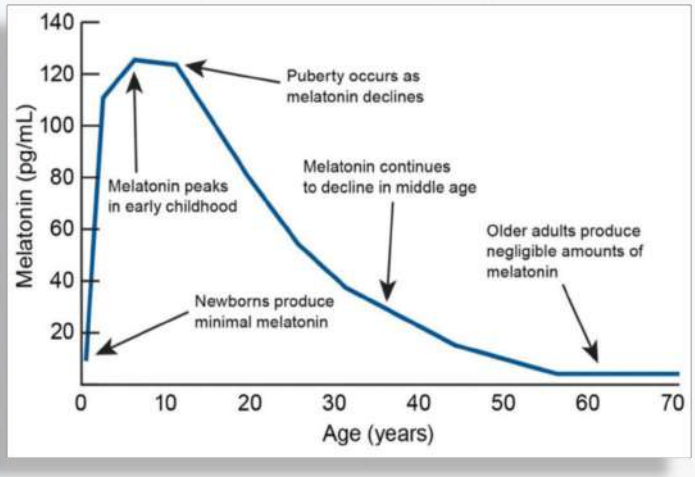
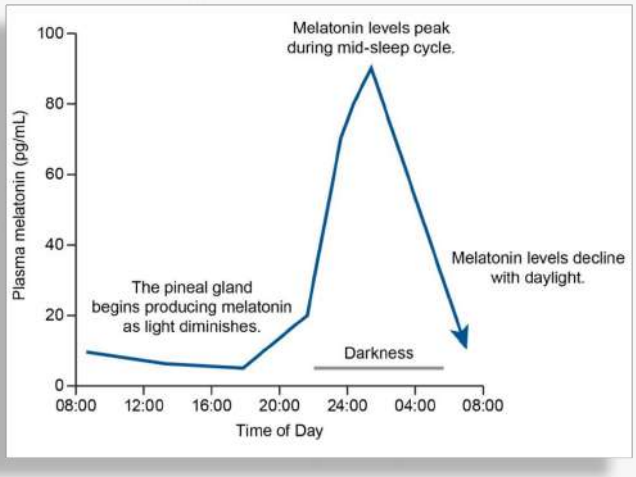
MELATONINA





Nutrients; 14(19):3934, 2022
doi: 10.3390/nu14193934

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Clinical pharmacokinetics of melatonin: a systematic review

Purpose: The aim of the review was to provide an overview of studies investigating the pharmacokinetics of exogenous melatonin in humans and if possible, to provide recommendations for clinical use.

Methods: The review was conducted in accordance to PRISMA guidelines. A systematic literature search was performed in PubMed and Embase databases. The pharmacokinetic variables included maximal plasma/serum concentration (Cmax), time to maximal plasma/serum concentration (Tmax), elimination half-life (T1/2), area-under-the-curve plasma/serum concentrations (AUC), clearance (Cl), volume of distribution (VD), and bioavailability.

Results: The literature search identified 392 records. Twenty-two studies were included in the review. Melatonin dosages varied between 0.3 and 100 mg and were administered either orally or intravenously. Cmax ranged from 72.1 (10 ml/h; 0.02 mg, IV) to 101,163 pg/ml (100 mg, oral). Tmax ranged between 15 (2 mg) and 210 min (10 mg). T1/2 ranged from 28 (0.005 mg, IV) to 126 min (4 mg, oral), whereas AUC ranged between 5400 (0.005 mg, IV) and 6.56 × 10(10) pg/ml × min (1 mg, oral). Cl ranged from 0.97 (0.005 mg, IV) to 132.50 L/min (6 mg, oral), whereas VD ranged between 35 (0.005 mg, IV) and 1602 L (4 mg, oral). Bioavailability of oral melatonin ranged from 9 to 33%. Pharmacokinetics was affected by age, caffeine, smoking, oral contraceptives, feeding status, and fluvoxamine. Critically ill patients displayed accelerated absorption and compromised elimination.

Conclusions: Despite methodological differences between the included studies, Tmax was approximately 50 min following oral immediate-release formulations of melatonin. T1/2 was 45 min in both administration routes. Cmax, AUC, Cl, and VD varied extensively between studies. Bioavailability of oral melatonin was approximately 15%.

MELATONINA

A biodisponibilidade da melatonina via oral é de aproximadamente 15% (9% a 33%).

Sua farmacocinética pode ser afetada por idade, cafeína, cigarro, anticoncepcionais, alimentação, dentre outros.

Eur J Clin Pharmacol; 71(8):901-909, 2015
doi: 10.1007/s00228-015-1873-4

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Nanotechnology-based advances in the efficient delivery of melatonin

Abstract

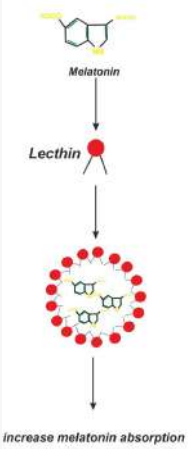
N-[2-(5-methoxy-1*H*-indol-3-yl) ethyl] or simply melatonin is a biogenic amine produced by pineal gland and recently recognized various other organs. Because of a broad range of biological function melatonin is considered as a therapeutic agent with high efficacy in the treatment of multiple disorders, such as cancer, degenerative disorders and immune disease. However, since melatonin can affect receptors on the cellular membrane, in the nucleus and can act as an anti-oxidant molecule, some unwanted effects may be observed after administration. Therefore, the entrapment of melatonin in biocompatible, biodegradable and safe nano-delivery systems can prevent its degradation in circulation; decrease its toxicity with increased half-life, enhanced pharmacokinetic profile leading to improved patient compliance. Because of this, nanoparticles have been used to deliver melatonin in multiple studies, and the present article aims to cumulatively illustrate their findings.

Keywords: Melatonin, Nano-delivery, Chitosan, Liposomes, PLGA, Solid lipid nanoparticles

O uso na forma de lipossomas previne sua degradação na circulação, diminui sua toxicidade com aumento da meia-vida e potencializa o perfil farmacocinético.

Cancer Cell Int; 22(1):43, 2022
doi: 10.1186/s12935-022-02472-7

MELATONINA



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SUPLEMENTAÇÃO EM **GOTAS BIOATIVAS**

INFORMAÇÃO NUTRICIONAL

Porções por embalagem: Cerca de 714
Porção: 0,042 ml (1 gota)

	0,042 ml	%VD*
Melatonina (mg)	0,21	

Não contém quantidades significativas de valor energético, carboidratos, açúcares totais, açúcares adicionados, proteínas, gorduras totais, gorduras saturadas, gorduras trans, fibras alimentares e sódio.

*Percentual de valores diários fornecidos pela porção.

Ingredientes:
Água, melatonina, agente de massa glicerol e emulsificante lecitina.
ALÉRGICOS: CONTÉM DERIVADOS DE SOJA.

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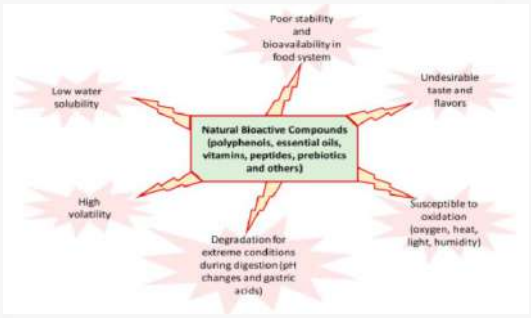
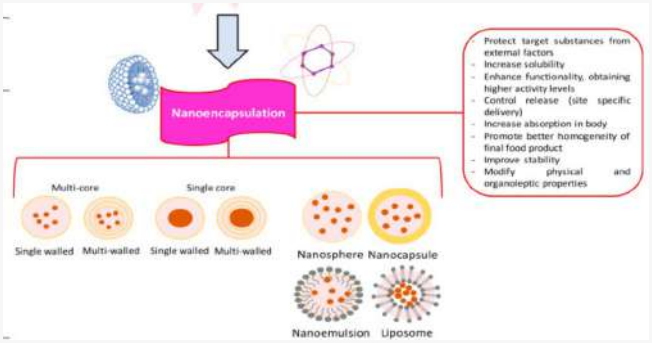
VANTAGENS DESSAS TECNOLOGIAS

- AUMENTO DA BIODISPONIBILIDADE
- AUMENTO DA ESTABILIDADE
- FÁCIL SOLUBILIZAÇÃO DE ATIVOS LIPOFÍLICOS
- COMPATIBILIDADE COM FORMULAÇÕES E ALIMENTOS AQUOSOS
- NOVA FORMA DE APRESENTAÇÃO
- NOVAS POSSIBILIDADES EM DOSAGENS





Molecules; 26(6):1547, 2021
doi: 10.3390/molecules26061547

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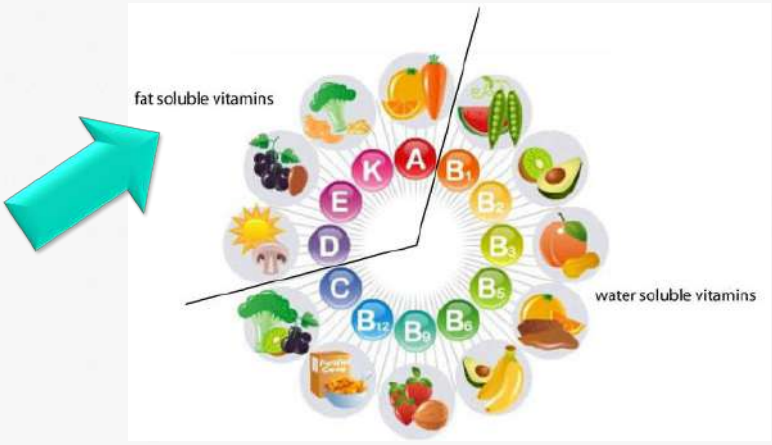
VITAMINAS LIPOSSOLÚVEIS



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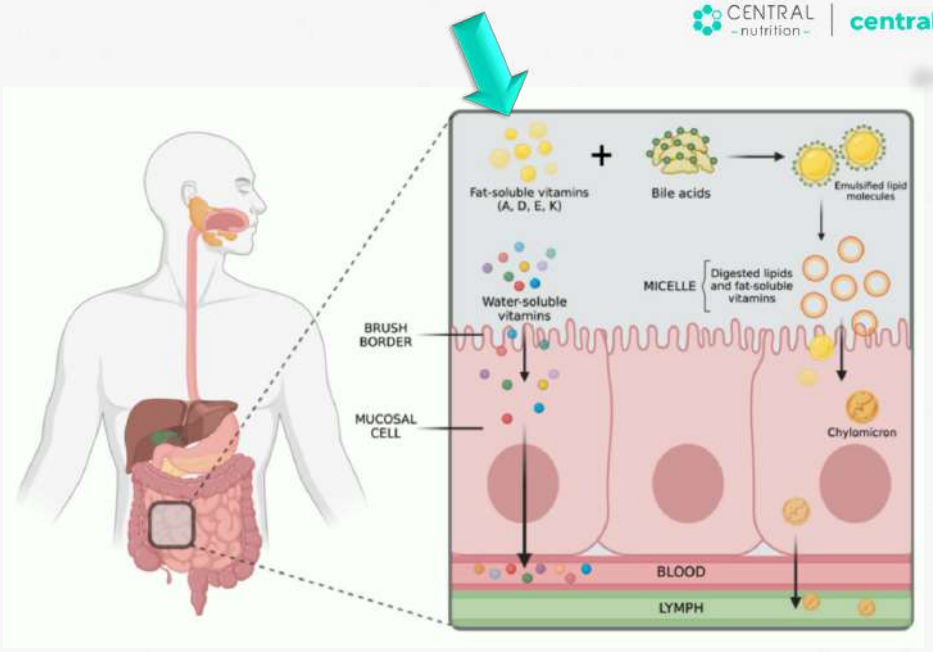

Cureus; 16(2):e55062, 2024
doi: 10.7759/cureus.55062

MASTERCLASS

SUPLEMENTAÇÃO EM **GOTAS BIOATIVAS**

INFORMAÇÃO NUTRICIONAL

Porções por embalagem: 450
Porção: 0,03 ml (1 gota)

	0,03 ml	%VD*
Vitamina A (µg)	135	17
Vitamina D (µg)	50	333
Vitamina E (mg)	2,3	15
Vitamina K (µg)	25	21

Não contém quantidades significativas de valor energético, carboidratos, açúcares totais, açúcares adicionados, proteínas, gorduras totais, gorduras saturadas, gorduras trans, fibras alimentares e sódio.

*Percentual de valores diários fornecidos pela porção.

UMA GOTA DE RESTAURE® CONTÉM:

VITAMINA D3 2000 UI
VITAMINA K2MK7 (menaquinona 7)
VITAMINA E na forma de tocoferóis/tocotrienóis
VITAMINA A

Ingredientes: Vitamina D3, Vitamina E, Vitamina K2, Vitamina A, óleo de amêndoas e óleo de laranja.

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Obrigado!

Prof. PhD Márcio Souza

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YouTube /MarcioNutricionista

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