1. Product card	ActiveCare drink 231

Triple-action supplementation as optimal help to maintaining daily vitality without chronic fatigue.

Short description:

Patented **microencapsulated iron** without side-effects + vitamin C from natural source for increased absorption of food iron & patented **Coenzyme Q10** for reducing stress at the cellular level & patented **grape seed extract** for additional strong antioxidant activity.

Active ingredients:

1. AB Fortis® - patented microencapsulated Fe^{3+} iron in alginate with high absorption and no side effects.
2. Acerola extract – natural source of vitamin C.
3. Coenzyme Q10Vital®
4. VinOseed® - grape seed extract with 95 % total polyphenols

Problem statement:

Ferrous salts, the most common iron supplements, have **numerous side effects** which include: heartburn, nausea, vomiting, diarrhoea, or constipation,[1] but also flatulence, abdominal pain, and black or tarry stools[2], metallic taste, staining of the teeth, or epigastric distress[3].
These are the main **causes for voluntary interruption of iron supplementation**.[4]

Evidence exists to suggest that reactive oxygen species induce muscular injury with a subsequent decrease in physical performance. **Supplementation with certain antioxidants is important for physically active individuals** to hasten recovery from fatigue and to prevent exercise damage.[5]

Coenzyme Q10 is an essential component of the mitochondrial electron transport chain and an antioxidant in plasma membranes and lipoproteins. **A significant reduction in the rate of CoQ biosynthesis has been proposed to occur during the aging process** and aging-associated diseases.[6]

Intended use:

Effective supplementation as optimal help to maintaining daily vitality without chronic fatigue.

[1] Hyder, S. M., Persson, L. A., Chowdhury, A. M., Ekström, E. C., Do side-effects reduce compliance to iron supplementation? A study of daily- and weekly-dose regimens in pregnancy, Journal of Health, Population and Nutrition, Vol. 20, Issue 2 (2002), pp. 175-179.
[2] Tolkien, Z., Stecher, L., Mander, A. P., Pereira, D. I. A., Powell, J. J., Ferrous Sulfate Supplementation Causes Significant Gastrointestinal Side-Effects in Adults: A Systematic Review and Meta-Analysis, PLoS ONE, Vol. 10, Issue 2 (2015), art. e0117383.
[3] Nguyen, M., Tadi, P., Iron Supplementation, StatPearls, Treasure Island, 2022, available at: https://www.ncbi.nlm.nih.gov/books/NBK557376/ (last consultation October 2022).
[4] Hyder, S. M., Persson, L. A., Chowdhury, A. M., Ekström, E. C., Do side-effects reduce compliance to iron supplementation? A study of daily- and weekly-dose regimens in pregnancy, Journal of Health, Population and Nutrition, Vol. 20, Issue 2 (2002), pp. 175-179.
[5] Drobnic, F., Lizarraga, M. A., Caballero-García, A., Cordova, A., Coenzyme Q10 Supplementation and Its Impact on Exercise and Sport Performance in Humans: A Recovery or a Performance-Enhancing Molecule? Nutrients, Vol. 14, Issue 9 (2022), art. 1811
[6] Hernández-Camacho, J. D., Bernier, M., López-Lluch, G., Navas, P., Coenzyme Q10 Supplementation in Aging and Disease, Frontiers in Physiology, Vol. 9 (2018), pp. 44.

Benefits:	
1. Optimized iron metabolism. 2. Extreme stability of supplemental iron. 3. High iron content of supplemental iron. 4. High absorption of supplemental iron. 5. High bioavailability of supplemental iron. 6. Additional intake of food-ingested iron due to vitamin C. 7. No side effects.	8. Solubility in aqueous media of Coenzyme Q10 which leads to better absorbtion. 9. High bioavailability of Coenzyme Q10. 10. Antioxidant activity of Coenzyme Q10. 11. Added grape seed extract for additional strong antioxidant activity.
Main target populations:	
1. Active sportspeople. 2. Older adults. 3. Vegans & vegetarians.	4. Women of reproductive age. 5. Pregnant women.

2. Longer product description

ActiveCare drink 231 are a blend of ingredients scientifically designed as optimal help to maintaining daily vitality without chronic fatigue. It has a triple action:

1. Optimal iron supplementation for a day without chronic fatigue due to anemia:
   - Microencapsulated Fe^{3+} iron provides iron directly to duodenum, thus avoiding side effects.
   - Added vitamin C enhances absorption of non-heme iron from ingested food.
2. Coenzyme Q10 as an essential component of the mitochondrial electron transport and for reducing stress at the cellular level through its antioxidative properties.
   - Water soluble Coenzyme Q10 Vital® for better absorption and high bioavailability.
3. Grape seed extract for additional strong antioxidant activity in both water- and fat-soluble phases.
   - Vinoseed® - grape seed extract with 95 % total polyphenols.

While heme iron is best absorbed, heme iron supplements are extremely dangerous because of ease of overdosing. Furthermore, they are not suitable for vegans and vegetarians.
Non-heme iron from food is extremely bio-unavailable.
Non-heme iron supplements are in the Fe^{2+} form which has good bioavailability but is very difficult for use in practice because of high rates of voluntary disruption of treatments by patients due to excessive side effects. The side effects come from the fact that reduction of iron is done in the stomach acid and the excess iron then floods the intestines.

Microencapsulated Fe^{3+} iron bypasses the stomach acid and provides iron directly to the intestinal mucose cells in duodenum:

- Dissolution of microencapsulation takes place in duodenum.
- Reduction of Fe^{3+} to Fe^{2+} is effected not by stomach acid but by the enzyme duodenal cytochrome *b* (Dcyt *b*) on the brush border of the duodenum cells.

Additional non-heme iron is absorbed from ingested food due to vitamin C that acidizes the stomach contents and enhances non-heme iron absorption.

Coenzyme Q10 (CoQ10) also referred to as ubiquinone, is a fat-soluble, vitamin-like molecule found naturally in every cellular membrane in our bodies. It plays an essential role in mitochondrial function as part of the electron transfer chain, which produces adenosine triphosphate (ATP), the energy currency of our cells. CoQ10 also has important antioxidant functions, preventing oxidation of lipids, proteins and DNA. CoQ10 also plays a role in regulating gene expression, in particular of genes involved in cell signalling, metabolism, inflammation, transport and transcription control. [7]

Coenzyme Q10Vital® is specially designed water-soluble formula for best absorbtion and high bioavailability.

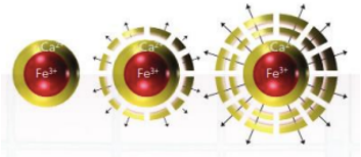
VinOseed® offers additional strong antioxidant activity and the ability to serv as free radical scavenger thanks to its high content in phenolic compounds as are oligomeric proanthocyanidins (OPCs), which are active in both water- and fat-soluble phases, whereas vitamins are only soluble in one or the other.

3. Health claims allowed by EFSA[8]

VITAMIN C:

- Vitamin C contributes to normal functioning of the nervous system.
- Vitamin C contributes to normal psychological function.
- Vitamin C contributes to the protection of cells from oxidative stress.
- Vitamin C contributes to the reduction of tiredness and fatigue.
- Vitamin C increases iron absorption.

4. Explanation of ingredients and their benefits

AB Fortis®	
1. Optimised iron metabolism	**2. Extreme stability**
Provides iron directly to the intestinal mucose cells in duodenum by avoiding the dissolution and reduction of Fe^{3+} into Fe^{2+} in the stomach: - Dissolution of microencapsulation takes place in duodenum. - Reduction of Fe^{3+} to Fe^{2+} is effected not by stomach acid but by the enzyme duodenal cytochrome *b* (Dcyt *b*) on the brush border of the duodenum cells.[9] 	- Excellent long-term stability (less than 1 % loss of iron in aqueous medium at 25°C for 12 months). - Withstands high pressure (less than 2 %loss of iron at 1,000 bar). - Withstands high temperature (less than 0.5 % loss of iron at 125°C for 3 h). - Incomparable stability during production process and on the shelf.

[7] Elgar, K. , Coenzyme Q10: A Review of Clinical Use and Efficacy, Nutritional Medicine Journal, Vol. 1, Issue 1, pp. 100-118.
[8] EU, Register of nutrition and health claims made on foods, V.3.6, available at: https://ec.europa.eu/food/safety/labelling_nutrition/claims/register/public (last consultation November 15, 2022).
[9] Ekmekcioglu, C., Feyertag, J., Marktl, W., A ferric reductase activity is found in brush border membrane vesicles isolated from Caco-2 cells, Journal of Nutrition, Vol. 126, Issue 9 (1996), pp. 2209-2217.

3. High iron content	4. High absorption
Standardised to contain 40% of elemental iron (ferrous sulphate contains around 36%).	Has at least as good absorption and bioavailability as ferrous sulphate, the best and most widely used iron supplement today.[10]
5. High bioavailability	**6. No side effects**
A clinical study showed that AB Fortis® was not only easily absorbable but that it also significantly incorporated into hemoglobin.[11]	- Avoids dissolution of iron in the mouth, thus eliminating bad taste and darkening of teeth. - Avoids release of free iron in the stomach and duodenum, thus practically eliminating side effects caused by excessive iron that feeds pathogenic gut bacteria.[12][13]

Vitamin C, from acerola extract

Acerola extract is natural source of Vitamin C, which increases absorption of additional non-heme iron from food.

Coenzyme Q10 Vital®

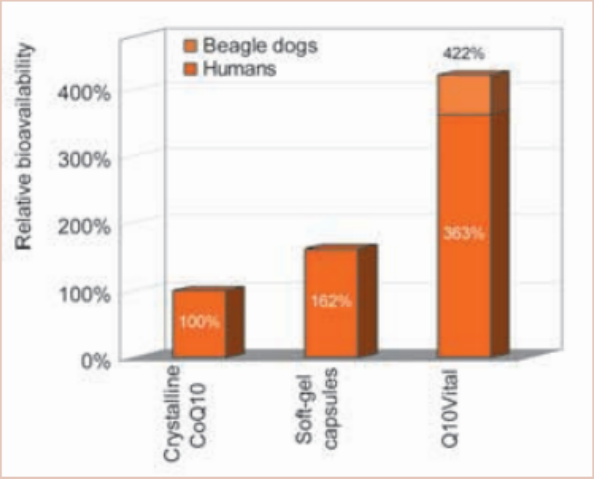
1. Solubility in aqueous media	2. High bioavailability
Every single molecule of lipophilic Q10 is entrapped in the lipophilic cavity of a β-cyclodextrin (β-CD) molecule, a starch derivative with a hydrophilic outer surface, **making it apparently hydrophilic and soluble in aqueous media**, which leads to **better absorbtion**.[14]	Studies have shown that **bioavailability of Q10Vital® reaches more than 400% of the bioavailability** of crystalline (basic, fat-soluble) CoQ10.[13,15,16]

[10] Contreras, C., Barnuevo, M. D., Guillen, I., Luque, A., Lazaro, E., Espadaler, J., Lopez-Roman, J., Villegas, J. A., Comparative study of the oral absorption of microencapsulated ferric saccharate and ferrous sulfate in humans, European Journal of Nutrition, Vol. 53 (2014), pp. 567–574.
[11] Lázaro, E., Santas, J., Rafecas, M., Recovery from dietary iron deficiency anaemia in rats by the intake of microencapsulated ferric saccharate, Journal of Food Science Technology, Vol. 54, Issue 9 (2017), pp. 2913-2918.
[12] Lázaro, E., Santas, J., Rafecas, M., Recovery from dietary iron deficiency anaemia in rats by the intake of microencapsulated ferric saccharate, Journal of Food Science Technology, Vol. 54, Issue 9 (2017), pp. 2913-2918.
[13] The clinical study on humans confirmed this, Contreras, C., Barnuevo, M. D., Guillen, I., Luque, A., Lazaro, E., Espadaler, J., Lopez-Roman, J., Villegas, J. A., Comparative study of the oral absorption of microencapsulated ferric saccharate and ferrous sulfate in humans, European Journal of Nutrition, Vol. 53 (2014), pp. 567–574.
[14] Žmitek, J., Žmitek, K., Pravst, I., Improving the bioavailability of coenzyme Q10 From theory to practice, Agro Food Industry Hi-Tech, Vol. 19, Issue 4 (2008), pp. 9-10.
[15] Žmitek, J., Šmidovnik, A., Fir, M., Prošek, M., Žmitek, K., Walczak, J., Pravst, I., Relative Bioavailability of Two Forms of a Novel Water-Soluble Coenzyme Q10, Annals of Nutrition & Metabolism, Vol. 52, Issue 4 (2008), pp. 281-287.
[16] Prosek, M., Butinar, J., Lukanc, B., Fir, M. M., Milivojevic, L., Krizman, M., Smidovnik, A., Bioavailability of water-soluble CoQ10 in beagle dogs, Journal of Pharmaceutical and Biomedical Analysis, Volume 47 (2008), pp. 918-922.

3. Powerul natural antioxidant

Twelve weeks of daily supplementation with 50 and 150 mg of Q10Vital® resulted in:
-limited seasonal deterioration of **viscoelasticity;**
-reduced visible signs of **ageing;**
-significantly reduced **wrinkles** and microrelief lines;
-improved skin **smoothness.**[17]

Figure 2. Relative bioavailability of three forms of CoQ10* (20, 27, 30)



*adopted from three separate studies and recalculated with crystalline CoQ10 as a reference product: a) Single-dose (SD) bioequivalence study of CoQ10 in soybean oil suspension (soft-gel capsules) and crystalline CoQ10 as a reference (human volunteers, 100 mg CoQ10) (27); b) SD bioequivalence study of water-soluble Q10Vital and soft-gel capsules as a reference (human volunteers, 60 mg CoQ10) (20); c) SD bioequivalence study of water-soluble Q10Vital and soft-gel capsules as a reference (beagle dogs, 30 mg CoQ10) (30)

Vinoseed® (95 % total polyphenols)

VinOseed® offers a **strong antioxidant activity** and the ability to serv as **free radical scavenger** thanks to its high content in phenolic compounds as are oligomeric proanthocyanidins (OPCs). Scientific studies have shown that the antioxidant power of proanthocyanidins is 20 times greater than vitamin E and 50 times greater than vitamin C.[18] Furthermore, grape seed OPCs are **active in both water and fat soluble phases**, whereas vitamins are only soluble in one or the other.

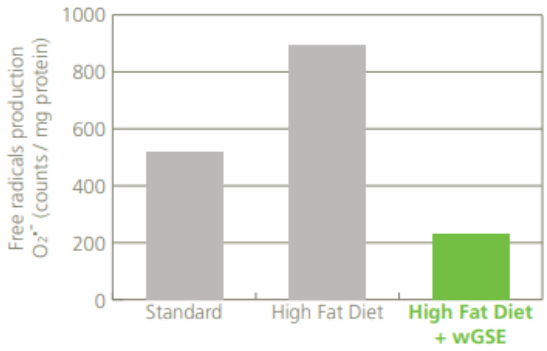
Through different and various studies, it was proved that the proanthocyanidin rich grape seed extract provides benefits against many diseases i.e. inflammation, cardiovascular disease, hypertension, diabetes, cancer, peptic ulcer, microbial infections, etc.[19]

Studies also showed that white Grape Seed Extract (GSE) could be involved in obesity-risk reduction:
- improves antioxidant status by **reducing free radicals production**;

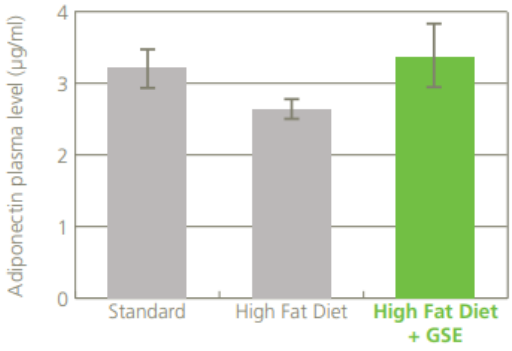
[17] Zmitek, K., Pogačnik, T., Mervic, L., Zmitek, J., Pravst, I., The effect of dietary intake of coenzyme Q10 on skin parameters and condition: Results of a randomised, placebo-controlled, double-blind study: The Effect of Dietary Intake of Coenzyme Q10 on Skin Parameters and Condition, BioFactors, Vol. 43 (2016).
[18] Shi, J., Yu, J., Pohorly, J. E., Kakuda, Y., Polyphenolics in grape seeds-biochemistry and functionality, Journal of Medicinal Food, Vol. 6, Issue 4 (2003), pp. 291-299.
[19] Gupta, M., Dey, S., Marbaniang, D., Pal, P., Ray, S., Mazumder, B. Grape seed extract: having a potential health benefits. Journal of Food Science and Technology. 2020 Vol. 57, Issue 4 (2020), pp.1205-1215.

- **limits cardiovascular risk** by increasing adiponectin expression (anti-inflammatory cytokine).[20,21]

Effect of white GSE supplementation on oxidative stress markers in case of induced obesity.



Effect of GSE supplementation on anti-inflammatory cytokine expression in case of high-fat diet.



There is a consensus that grape seed proanthocyanidins can contribute to a microbial ecology and modulate gut microbiota and with human health benefits, and thus show promise to use as a nutraceutical.[22]

[20] Decorde, K., Teissedre, P-L., Sutra, T., Ventura, E., Cristol, J., Rouanet, J-M. Chardonnay grape seed procyanidin extract supplementation prevents high-fat diet-induced obesity in hamsters by improving adipokine imbalance and oxidative stress markers, Molecular nutrition & food research, Vol. 53, Issue 5 (2009), pp. 659-666.

[21] Terra, X., Montagut, G., Bustos, M., Llopiz, N., Ardèvol, A., Bladé, C., Fernández-Larrea, J., Pujadas, G., Salvadó, J., Arola, L., Blay, M., Grape-seed procyanidins prevent low-grade inflammation by modulating cytokine expression in rats fed a high-fat diet, The Journal of Nutritional Biochemistry, Vol. 20, Issue 3 (2009), pp. 210-218.

[22] Unusan, N., Proanthocyanidins in grape seeds: An updated review of their health benefits and potential uses in the food industry, Journal of Functional Foods, Volume 67 (2020), art. 103861.

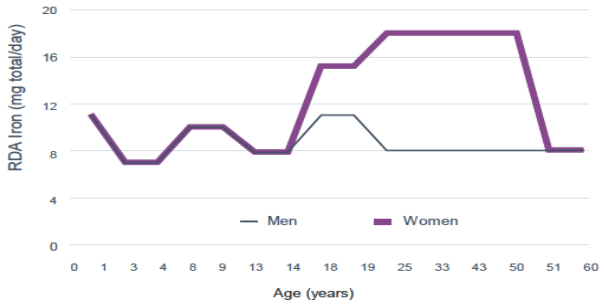
5. Explanation of the need for iron and coenzyme Q10 supplementation in different target populations

WOMEN

Women's need for iron is significantly higher

MENSTRUAL LOSS OF IRON

Women of reproductive age require twice the amount of iron as similarly-aged men.[23]



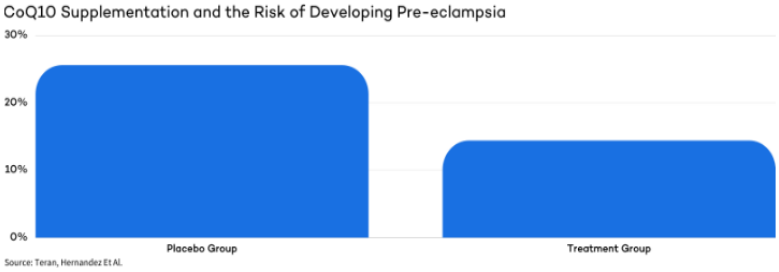
Source: IFF Health

PREGNANCY

The average Western diet is not sufficient to meet the needs of pregnancy.[24]

Oral supplementation of CoQ10 may increase clinical pregnancy when compared with placebo or no-treatment, in women with infertility undergoing assisted reproductive technologies procedures, without an effect on live birth or miscarriage rates.[25]

The effect of CoQ10 supplementation on women at an increased risk of developing pre-eclampsia was investigated. Women received 200 mg CoQ10 treatment from 20 weeks of pregnancy until delivery. The overall rate of pre-eclampsia in the study was 20 %. 25.6 % of the placebo group developed pre-eclampsia, compared with only 14.4 % of the CoQ10 treatment group women. Researchers determined that the difference between the two groups was significant and that supplementation with CoQ10 reduced the risk of developing pre-eclampsia.[26]



While research surrounding CoQ10 and pregnancy is limited, most studies indicate CoQ10 is usually safe to take during pregnancy. However, you should consult your doctor to ensure that taking CoQ10 is safe for you, especially together with all medications and other supplements.

[12] Ems, T., St Lucia, K., Huecker, M.R., Biochemistry, Iron Absorption, StatPearls, Treasure Island, 2022 available at: https://pubmed.ncbi.nlm.nih.gov/28846259/ (last consultation October 2022).
[13] Lee, A.I., Okam, M. M., Anemia in pregnancy, Hematology, Oncology Clinics of North America, Vol. 25, Issue 2 (2011), pp. 241-59.
[25] Florou, P., Anagnostis, P., Theocharis, P., Chourdakis, M., Goulis, D. G., Does coenzyme Q10 supplementation improve fertility outcomes in women undergoing assisted reproductive technology procedures? A systematic review and meta-analysis of randomized-controlled trials, Journal of Assisted Reproduction and Genetics, Vol. 37, Issue 10 (2020), pp. 2377-2387.
[26] Teran, E., Hernandez, I., Nieto, B., Tavara, R., Ocampo, J. E., Calle, A., Coenzyme Q10 supplementation during pregnancy reduces the risk of pre-eclampsia, International Journal of Gynaecology and Obstetrics, Vol. 105, Issue 1 (2009), pp. 43-45.

VEGANS & VEGETARIANS

EXTREMELY LOW BIOAVAILABILITY OF NON-HEME IRON IN PLANT-BASED FOODS

The iron status of vegans and vegetarians is compromised by:
- the absence of highly bioavailable heme-iron in meatless diets.
- the inhibiting effect of plant foods on non-heme iron bioavailability.[27]

SPORTSPEOPLE & RESPONSE TO EXERCISE

INCREASED HEMOGLOBINE PRODUCTION, SWEATING, AND INFLAMMATION[2829]

Sports increase the need for oxygen in the muscles, which increases hemoglobine production and thus the need for iron.

Sweating may induce losses of up to 2.5 micrograms of iron per liter sweat.[30]

Sport induced inflammation increases hepcidin levels, an iron regulatory protein, which blocks absorption of iron in the intestines.[31]

Evidence exists to suggest that reactive oxygen species induce muscular injury with a subsequent decrease in physical performance. Supplementation with certain antioxidants is important for physically active individuals to hasten recovery from fatigue and to prevent exercise damage. From the evaluation of the various studies reviewed it can be concluded that the use of Coenzyme Q10 seems to offer a good profile in the control of an oxidative pattern with a certain anti-inflammatory activity at the cellular level in response to exercise in the various populations studied. It can therefore be seen as a protective and recuperative substance.[32]

ANEMIA, CoQ10 BIOSYNTHESIS, AGING & OLDER ADULTS

IMPORTANT AGE-RELATED COMORBIDITY FACTORS

After adults reach 50 years, prevalence of anemia increases and exceeds 20% in those 85 years and older. In nursing homes, anemia is present in 48% to 63% of residents.[33] Men are at a higher risk of age-related anemia.[34]

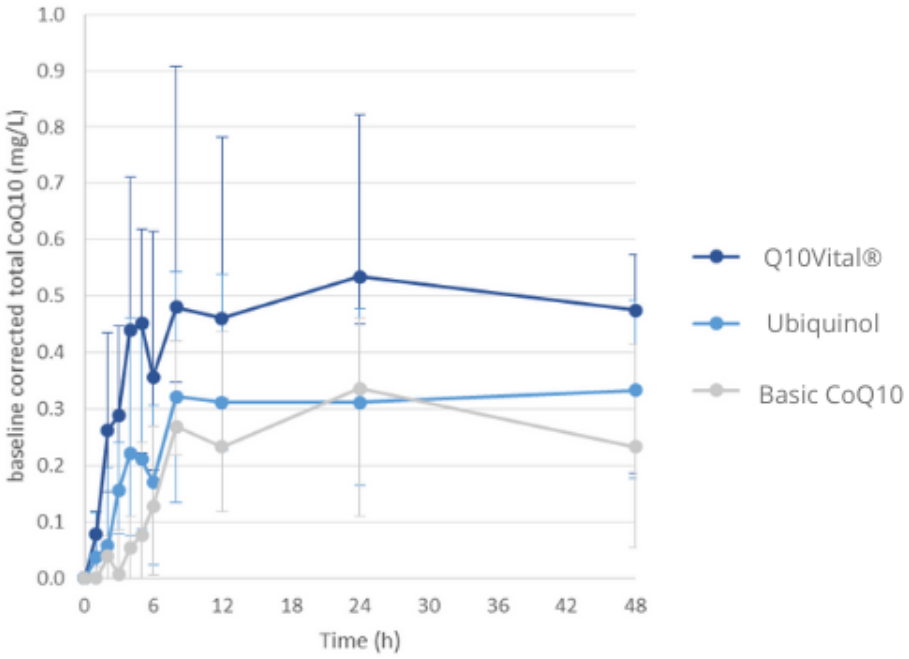
Coenzyme Q10 is an essential component of the mitochondrial electron transport chain and an antioxidant in plasma membranes and lipoproteins. A significant reduction in the rate of CoQ biosynthesis has been proposed to occur during the aging process and aging-associated diseases. There is evidence that supplementation positively affects mitochondrial deficiency syndrome and the symptoms of aging based

[15] Haider, L. M., Schwingshackl, L., Hoffmann, G., Ekmekcioglu, C., The effect of vegetarian diets on iron status in adults: A systematic review and meta-analysis, Critical Review in Food Science and Nutrition, Vol.58, Issue 8 (2018), pp. 1359-1374.
[17] Damian, M. T., Vulturar, R., Login, C.C., Damian, L., Chis, A., Bojan, A., Anemia in Sports: A Narrative Review, Life (Basel), Vol 11, Issue 9 (2021), art. 987.
[18] Clénin, G., Cordes, M., Huber, A., Schumacher, Y. O., Noack, P., Scales, J., Kriemler, S., Iron deficiency in sports - definition, influence on performance and therapy, Swiss Medical Weekly, Vol. 145 (2015), art. w14196.
[19] Brune, M., Magnusson, B., Persson, H., Hallberg, L., Iron losses in sweat, American Journal of Clinical Nutrition, Vol. 43 (1986), pp. 438–443.
[20] Dahlquist, D. T., Stellingwerff, T., Dieter, B. P., Effects of macro- and micronutrients on exercise-induced hepcidin response in highly trained endurance athletes, Applied Physiology, Nutrition and Metabolism, Vol. 42 (2017), pp. 1036–1043.
[32] Drobnic, F., Lizarraga, M. A., Caballero-García, A., Cordova, A., Coenzyme Q10 Supplementation and Its Impact on Exercise and Sport Performance in Humans: A Recovery or a Performance-Enhancing Molecule? Nutrients, Vol. 14, Issue 9 (2022), art. 1811
[21] Patel, K. V., Epidemiology of anemia in older adults, Seminal Hematology, Vol. 45, No. 4 (2008), pp. 210-217.
[22] Salive, M. E., Cornoni-Huntley, J., Guralnik, J. M., Phillips, C. L., Wallace, R. B., Ostfeld, A. M., et al. Anemia and hemoglobin levels in older persons: relationship with age, gender, and health status, Journal of American Geriatric Society, Vol. 40 (1992), pp. 489-496.

mainly on improvements in bioenergetics. Cardiovascular disease and inflammation are alleviated by the antioxidant effect of CoQ10.[35]

The study involved 3 different CoQ10 forms: ubiquinol, ubiquinone (Q10Vital®) and basic CoQ10 confirmed superior bioavailability of Q10Vital® compared to standard product as well as compared to ubiquinol. Bioavailability of Q10Vital® have been proven to be superior **even in older adults**, which are believed to have limited absorption of nutrients in the digestive system.

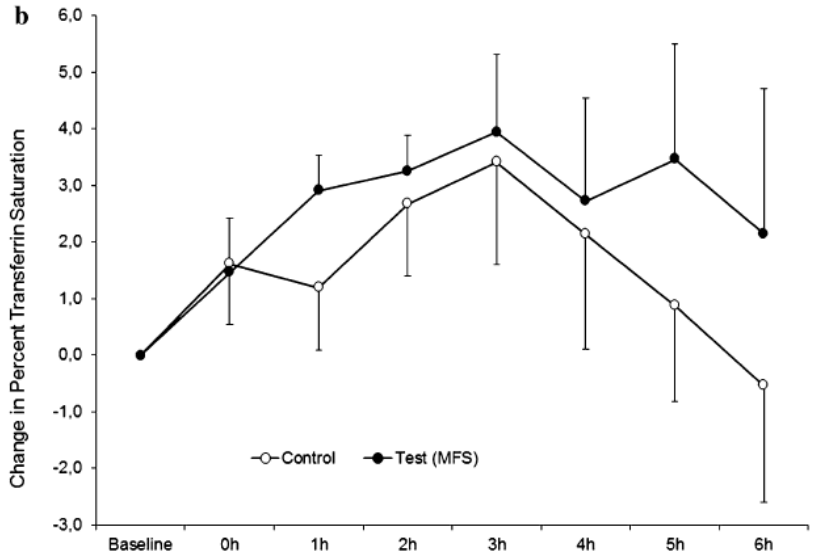
Ubiquinone (oxidized form of CoQ10) is normally reduced to ubiquinol during the absorption in the intestine and several marketing activities have tried to imply that with older people the transformation of ubiquinone to ubiquinol is very poor. The recent clinical study on older adults, comparing Q10Vital® (ubiquinone) and ubiquinol, showed no significant differences in the redox status of the absorbed CoQ10 – 90 % of all absorbed CoQ10 in the blood was shown in the reduced form. Meaning that CoQ10 appears in the blood almost exclusively as ubiquinol, even when ingested as ubiquinone by older adults.[36]



It was found that proanthocyanidins from grape seed extracts protect against age-related mental deterioration and depression by inducing hypothalamic-pituitaryadrenal axis action, serotonergic conveyance, and hippocampal neurogenesis. Proanthocyanidins also elevate Sirtuin 1 expression, which is recognized as an anti-aging agent that extends life span. Moreover, they possess tyrosinase inhibition activity and can reduce hyperpigmentation symptoms.[37]

[35] Hernández-Camacho, J. D., Bernier, M., López-Lluch, G., Navas, P., Coenzyme Q10 Supplementation in Aging and Disease, Frontiers in Physiology, Vol. 9 (2018), pp. 44.
[36] Pravst, I., Rodríguez-Aguilera, J., Cortés, A., Jazbar, J., Locatelli, I., Hristov, H., Zmitek, K., Comparative Bioavailability of Different Coenzyme Q10 Formulations in Healthy Elderly Individuals, Nutrients, Vol. 12, Issue 3 (2020), art. 784.
[37] Unusan, N., Proanthocyanidins in grape seeds: An updated review of their health benefits and potential uses in the food industry, Journal of Functional Foods, Volume 67 (2020), art. 103861.

6. Results on absorption of AB Fortis® in a clinical study on humans



Increase in transferrin saturation (transporters of iron throughout the body indicating that iron was absorbed by the body).[38]

7. Clinical studies

Lázaro, E., Santas, J., Rafecas, M., Recovery from dietary iron deficiency anaemia in rats by the intake of microencapsulated ferric saccharate, Journal of Food Science Technology, Vol. 54, Issue 9 (2017), pp. 2913-2918.

Contreras, C., Barnuevo, M. D., Guillen, I., Luque, A., Lazaro, E., Espadaler, J., Lopez-Roman, J., Villegas, J. A., Comparative study of the oral absorption of microencapsulated ferric saccharate and ferrous sulfate in humans, European Journal of Nutrition, Vol. 53 (2014), pp. 567–574.

Friling, M., García-Muñoz, A. M., Perrinjaquet-Moccetti, T., Victoria-Montesinos, D., Pérez-Piñero, S., Abellán-Ruiz, M. S., Luque-Rubia, A. J., García-Guillén, A. I., Cánovas, F., Ivanir, E., Tolerability of Oral Supplementation with Microencapsulated Ferric Saccharate Compared to Ferrous Sulphate in Healthy Premenopausal Woman: A Crossover, Randomized, Double-Blind Clinical Trial, International Journal of Molecular Sciences, Vol. 23, Issue 20 (2022), art. 12282.

Pravst, I., Rodríguez-Aguilera, J., Cortés, A., Jazbar, J., Locatelli, I., Hristov, H., Zmitek, K., Comparative Bioavailability of Different Coenzyme Q10 Formulations in Healthy Elderly Individuals, Nutrients, Vol. 12, Issue 3 (2020), art. 784.

Teran, E., Hernandez, I., Nieto, B., Tavara, R., Ocampo, J. E., Calle, A., Coenzyme Q10 supplementation during pregnancy reduces the risk of pre-eclampsia, International Journal of Gynaecology and Obstetrics, Vol. 105, Issue 1 (2009), pp. 43-45.

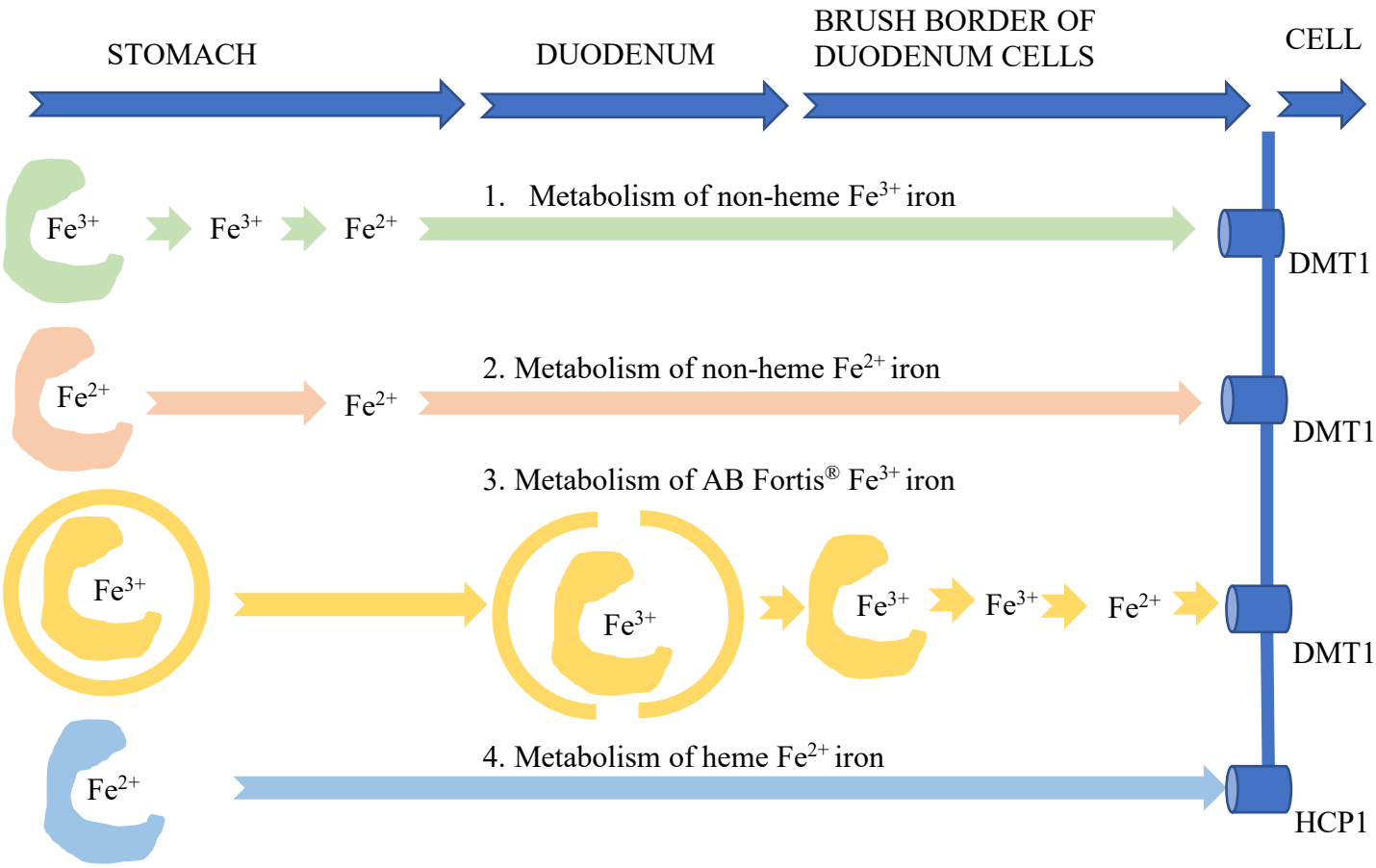
[23] Contreras, C., Barnuevo, M. D., Guillen, I., Luque, A., Lazaro, E., Espadaler, J., Lopez-Roman, J., Villegas, J. A., Comparative study of the oral absorption of microencapsulated ferric saccharate and ferrous sulfate in humans, European Journal of Nutrition, Vol. 53 (2014), pp. 567–574.

8. Comparative table of different forms of iron

Type	Heme iron	Non-heme iron		
		Ferric iron	**Ferrous iron**	**AB Fortis® -Ferric iron**
Chemical form	Fe^{2+} Ferrous cation trapped in a heme, a component of hemoglobyn	Fe^{3+} Ferric cation in different forms	Fe^{2+} Ferrous cation in different forms, mostly ferrous sulphate	Fe^{3+} Ferric cation in saccharate microencapsulated in calcium alginate
Sources	Animal food sources	Plants	Anorganic	Anorganic
Stability	Low	Good	Low	Excellent
Oxidation	High	Low	High	Low
Absorption	Very good	Very bad	Very good	Very good
Bioavailability	Very good	Very bad	Very good	Very good
Dependance on food regime	No dependance	Extreme dependance	Little dependance	No dependance
Release time	Ready-to-use form	Slow release	Fast release OR Slow release if microencapsulated	Slow release
Side effects	High risk of overdose	No side effects	Many and strong[39]	No side effects
Problems with supplementation	Very problematic due to severe risk of overdose. Not useful for vegans & vegetarians.	Not useful due to low bioavailability	Very problematic due to severe side effects.	No side effects. Great bioavailability.

[24] Hyder, S. M., Persson, L. A., Chowdhury, A. M., Ekström, E. C., Do side-effects reduce compliance to iron supplementation? A study of daily- and weekly-dose regimens in pregnancy, Journal of Health, Population and Nutrition, Vol. 20, Issue 2 (2002), pp. 175-179;
Tolkien, Z., Stecher, L., Mander, A. P., Pereira, D. I. A., Powell, J. J., Ferrous Sulfate Supplementation Causes Significant Gastrointestinal Side-Effects in Adults: A Systematic Review and Meta-Analysis, PLoS ONE, Vol. 10, Issue 2 (2015), art. e0117383.
Nguyen, M., Tadi, P., Iron Supplementation, StatPearls, Treasure Island, 2022, available at: https://www.ncbi.nlm.nih.gov/books/NBK557376/ (last consultation October 2022).

9. Schematic comparison of metabolic processes of different forms of iron



1. Metabolism of non-heme Fe^{3+} iron

Fe^{3+} released from the ligand in the stomach acid.
Fe^{3+} reduced into Fe^{2+} by the stomach acid (strong influence of diet and basically no absorption of iron).
Fe^{2+} transported directly to Divalent Metal Transporter (DMT1) through the membrane of the intestinal cells.

2. Metabolism of non-heme Fe^{2+} iron

Fe^{2+} released from the ligand in the stomach acid that continues the journey to the duodenum. Can flood the intestines with excess iron and cause gastric distress.

3. Metabolism of AB Fortis® Fe^{3+} iron

AB Fortis Fe^{3+} protected from gastric acid by calcium alginate.
Ferric saccharate released from the alginate in the alkaline environment of duodenum.
Fe^{3+} released from ferric saccharate in duodenum.
Fe^{3+} reduced into Fe^{2+} on the brush borders of duodenum cells.
Fe^{2+} transported directly by Divalent Metal Transporter (DMT1) through the membrane of intestinal cells.

4. Metabolism of heme Fe^{2+} iron

Heme Fe^{2+} transported directly by heme-specific Heme Carrier Protein (HCP1) through the membrane of the intestinal cells. As HCP1 is heme-specific absorption is excellent, but that means the risk of overdose is also extremely high.