Absorption, metabolism and secretion of tocopherol stereoisomers in dairy cows

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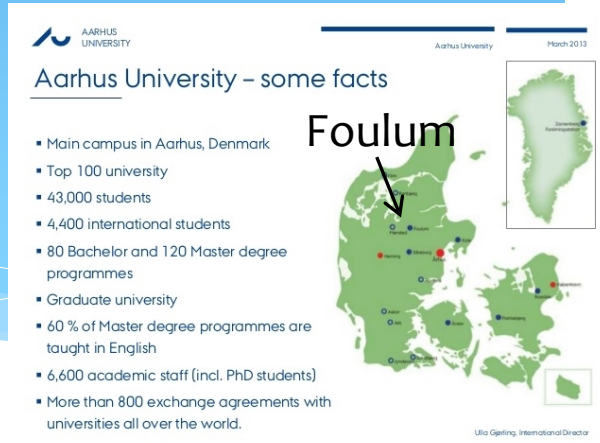

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Vitamin E

Vitamin E is essential for integrity and optimum function of the:

- Reproductive
- Muscular
- Circulatory
- Nervous
- immune

} system

(McDowell, 2000)

Relationship between vitamin E status, oxidative stability of milk and optimal immune function

Plasma µg/ml	Optimal immune function	Milk µg/g	Oxidation risk	Milk fat µg/g
>4	Optimal	>1.2	Very little	>30
3-4	Acceptable	0.8-1.2	Little	20-30
1-3	Slight deficiency	0.6-0.8	Risk	15-20
<1	Absolute deficiency	<0.6	Great	<15

(Knudsen et al. 2001)

Vitamin E requirement

Dairy cows

Requirements for vitamins are difficult to establish because measuring vitamins in feeds can be difficult. Vitamins can be destroyed or synthesized in the rumen, and responses to changes in vitamin supply is often very subtle and may take months to observe (Weiss 2014).

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IU/Day[1]	NRC	Danish[2]	IU/kg DMI
Dry cows	1000	960	≈100
Lactating cows	500	480	≈20
Close up		1800	≈200

[1])600 kg cow

[2])SEGES, 2022

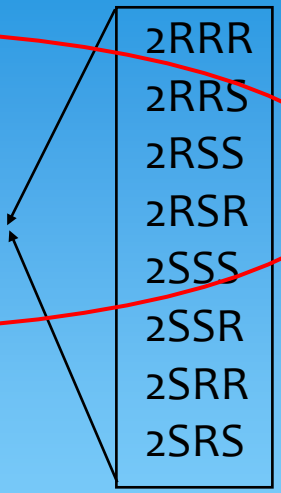
Vitamin E active compounds

- α-Tocopherol

- β-Tocopherol
- γ-Tocopherol
- δ-Tocopherol
- The corresponding tocotrienoles

Vitamin E active compounds

- RRR-α-tocopherol
- All-*rac*-α-tocopherol



- β-Tocopherol
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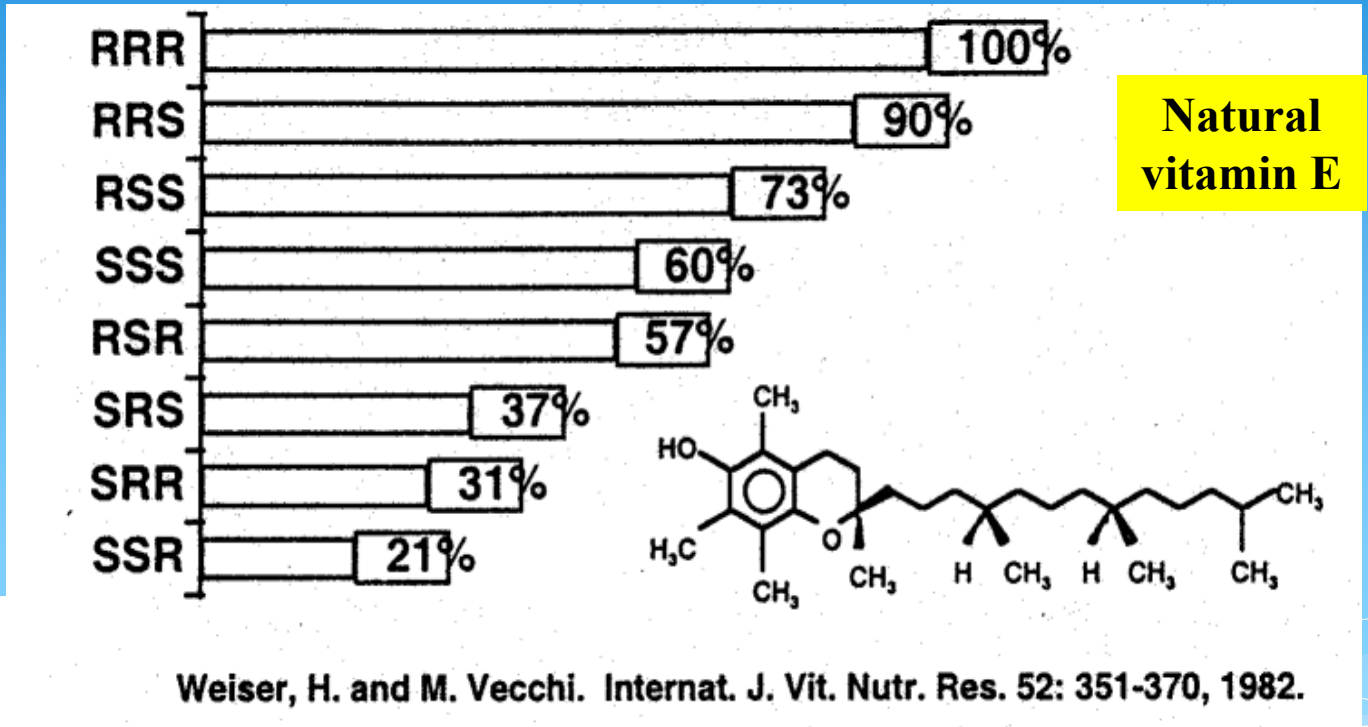
- δ-Tocopherol
- The corresponding tocotrienoles

Biological activity of the 8 stereoisomers of *all-rac*-α-tocopherol determined by the rat resorption gestation test



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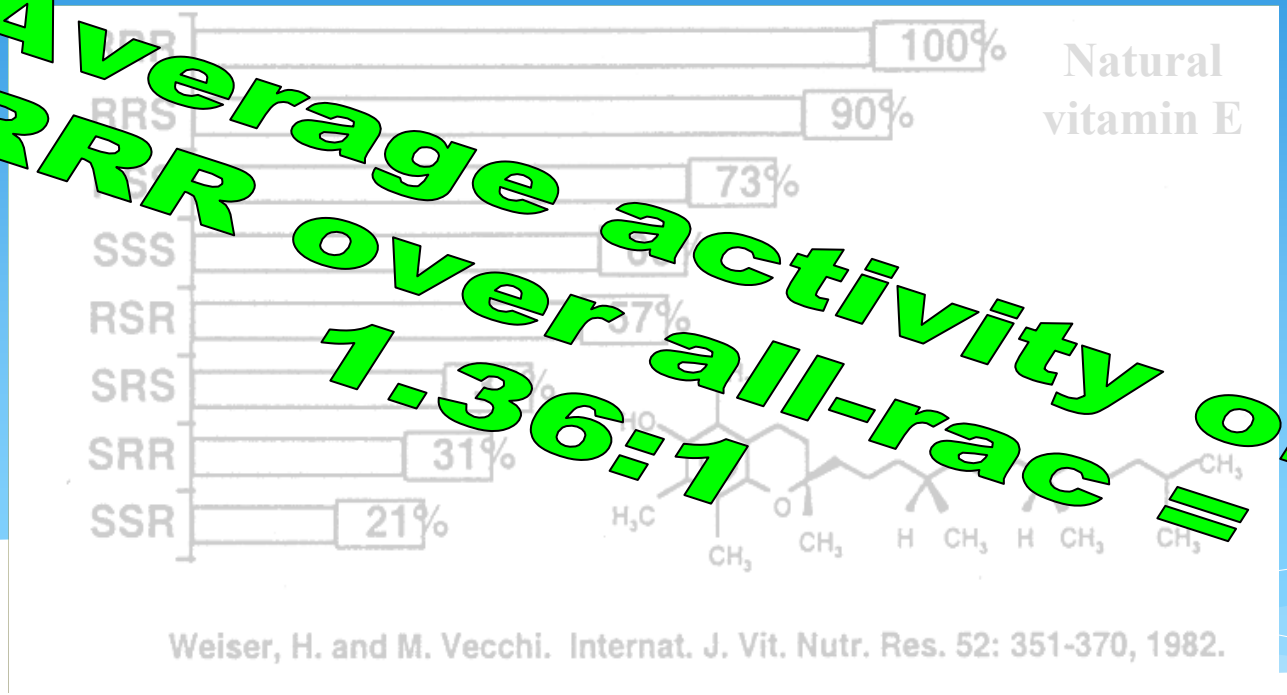
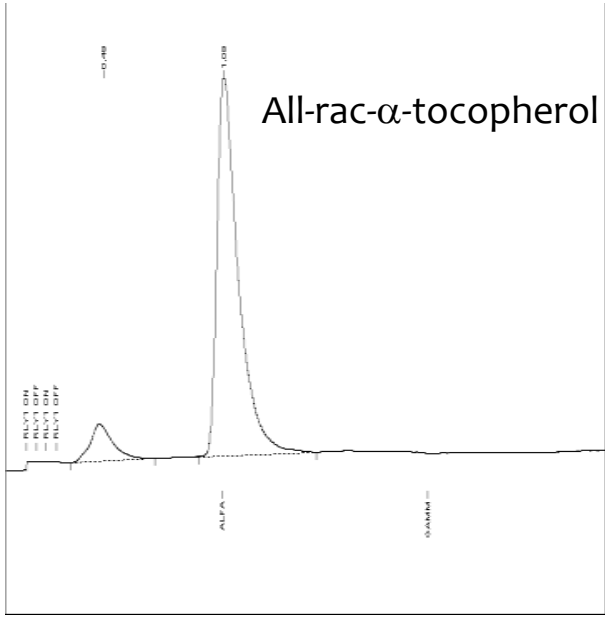


Average activity of RRR over all-rac = 1.36:1

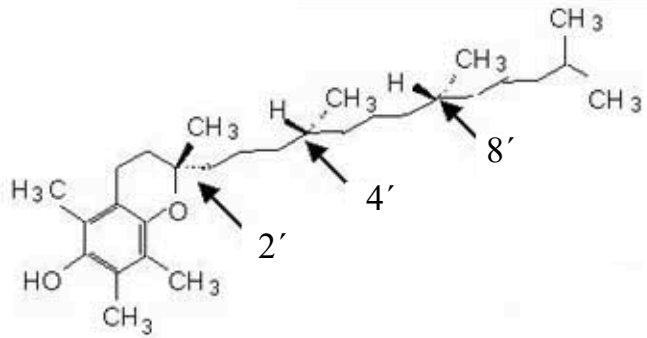
Analysis of α-tocopherol by HPLC

Conventional method



Separation of stereoisomers of α-tocopherol as methyl ethers by chiral column chromatography

The 4 Synthetic forms
with 2S configuration
2SR/SR/S-α-tocopherol

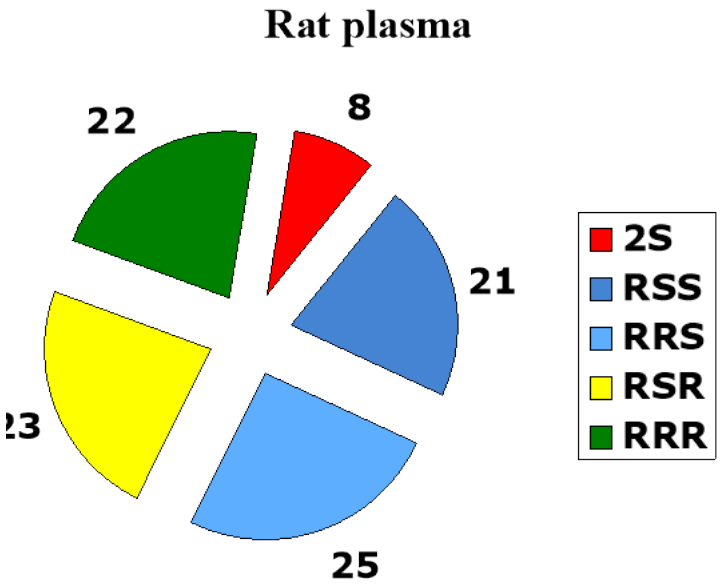


The 4 2R isomers
Natural

RSS RRS RRR RSR

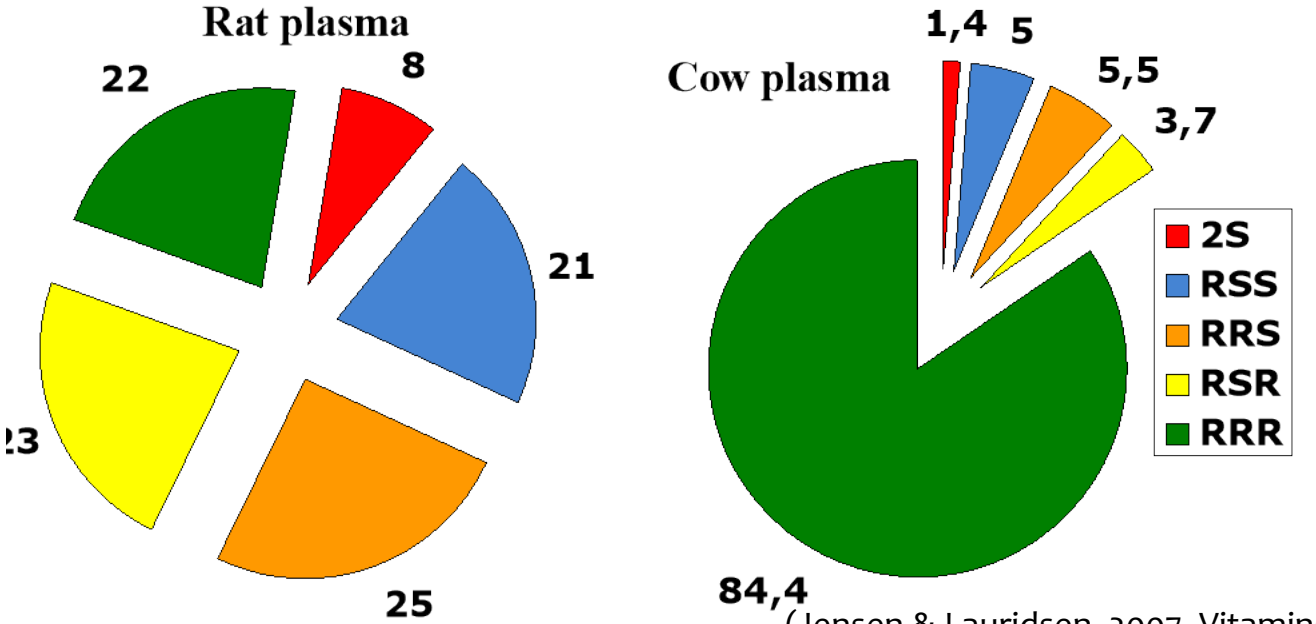
(Jensen & Lauridsen, 2007, Vitamins and Hormones)

Distribution of α-tocopherol stereoisomers in rat plasma fed *all-rac*-α-tocopheryl acetate



(Jensen & Lauridsen, 2007, Vitamins and Hormones)

Distribution of α-tocopherol stereoisomers in rat and cow plasma (Cows fed 3000 mg *all-rac*-α-tocopheryl acetate / day for 16 days)



(Jensen & Lauridsen, 2007, Vitamins and Hormones)

The responsible molecule for differences in plasma distribution of α-tocopherol stereoisomers is α-tocopherol transfer protein (α-TTP)

The affinity of α-TTP differs bettween animal species

Differences in plasma distribution of α-tocopherol stereoisomers between rats and cattle indicate different biological activity between animal species

Therefore it is relevant to study absorption, metabolism and secretion of tocopherol stereoisomers in dairy cows

Vitamin E sources

Dairy cows

Supplements

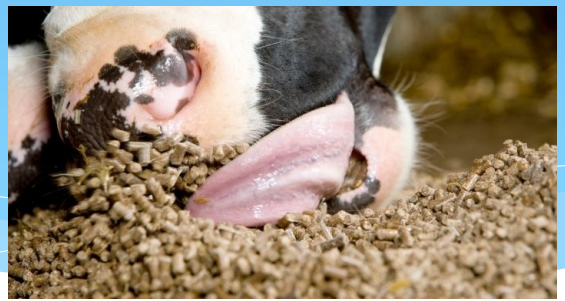
All-rac-α-Tocopheryl acetate
(Synthetic α-Tocopherol)
RRR-α-Tocopheryl acetate
RRR-α-Tocopherol

Roughage

RRR-α-Tocopherol

Concentrate

RRR-α-Tocopherol
RRR-α-Tocotrienol
RRR-γ-Tocopherol



Example of sources and amount of vitamin E in a high roughage dairy cow diet DMI 21.6 kg/day

Feed	g/kg DM	Synthetic α-tocopherol	RRR-α-Tocopherol	RRR-α-Tocotrienol	RRR-γ-Tocopherol
		Daily intake, mg			
Oat grain	217,1		23	**62**	7
Toasted fava beans	165.2		7	1	**144**
Grass clover silage	609		**752**		84
Mineral and vitamin supplements	8.70	**1040**	130		

(Lashkari et al. 2023, Animal Nutrition)

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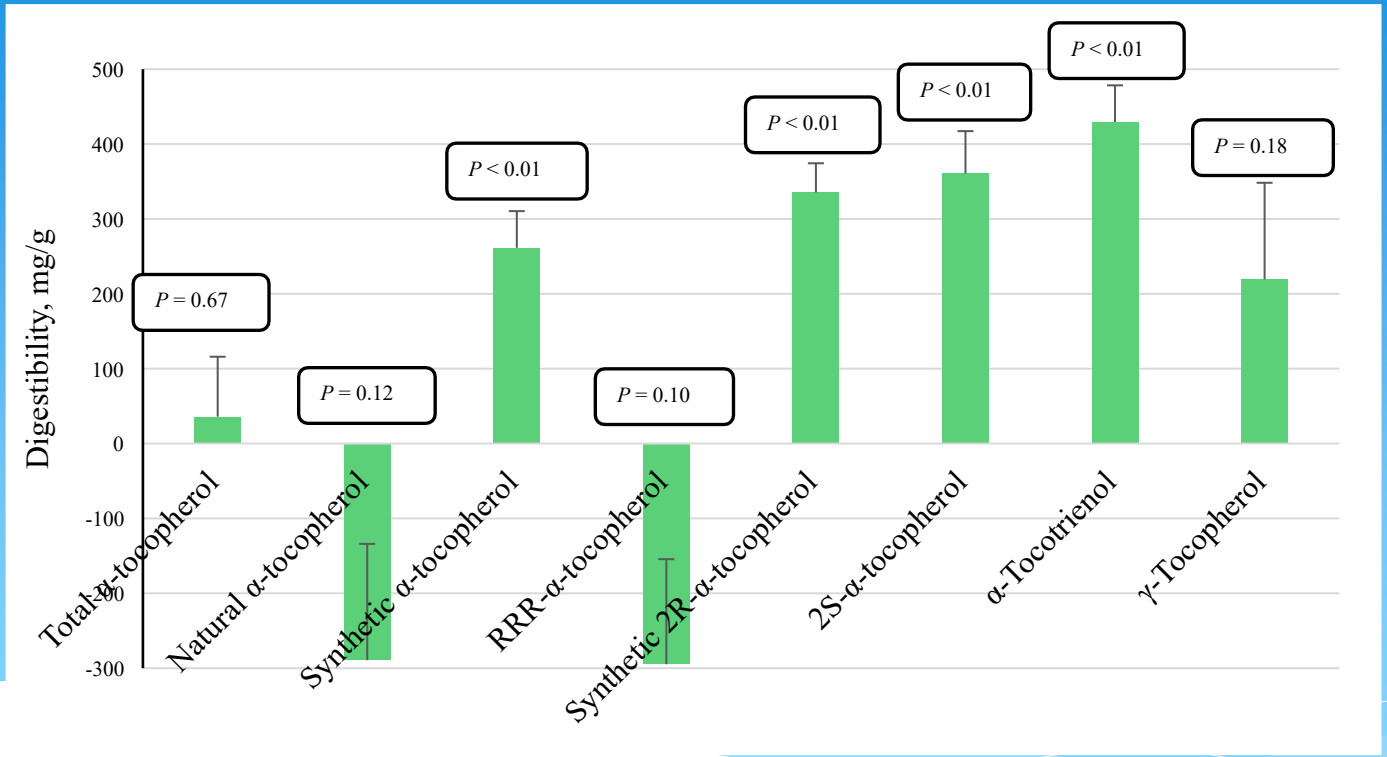
Tocopherol intake and balance in the digestive tract DMI 21.6 kg/day

Site	Total α-tocopherol	Synthetic α-tocopherol	RRR-α-Tocopherol	RRR-α-Tocotrienol	RRR-γ-Tocopherol
	Daily balance, mg				
Intake	1808	1021	915	72	235
Rumen	153	292	-184	40	61
Small intestine	591	228	420	16	62
Feed-ileum	744	520	236	56	123

(Lashkari et al. 2023, Animal Nutrition)

Digestibility of tocopherols in the rumen



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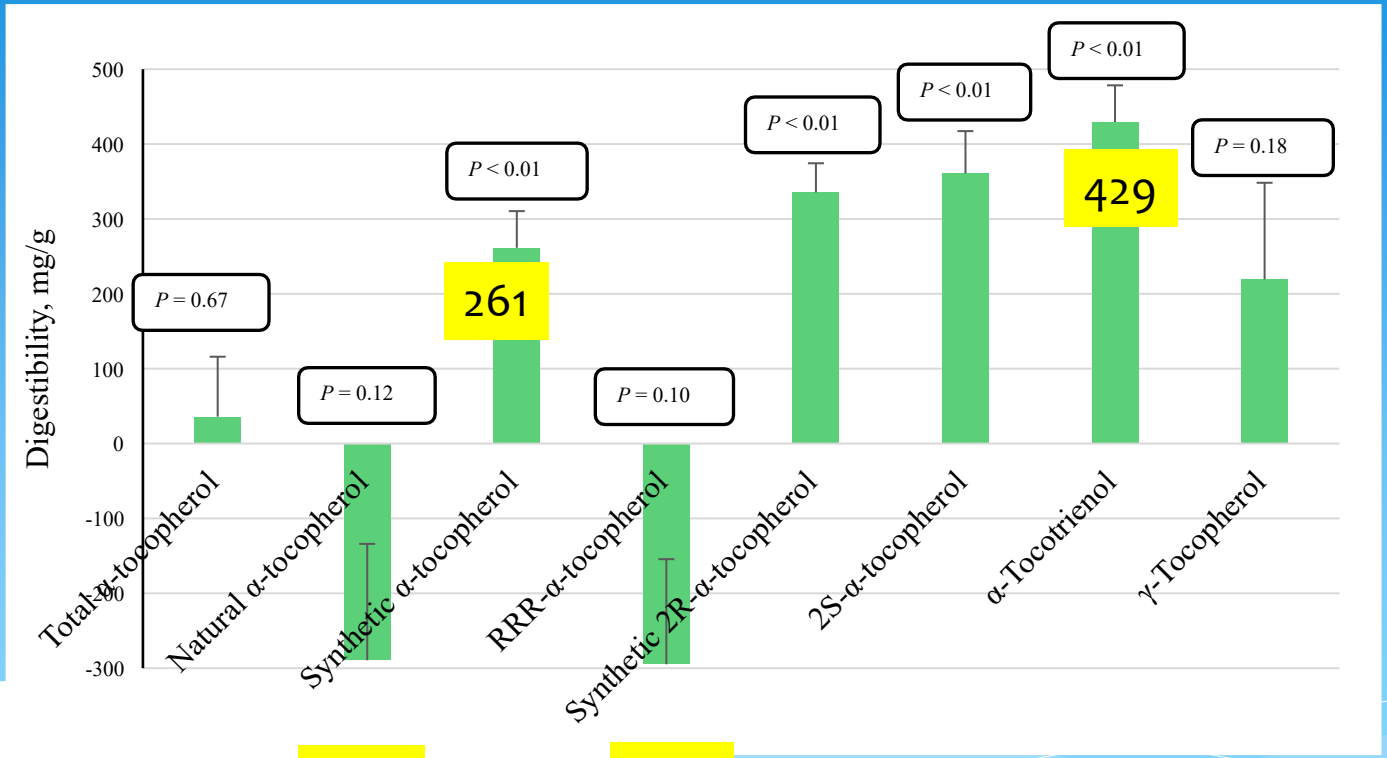

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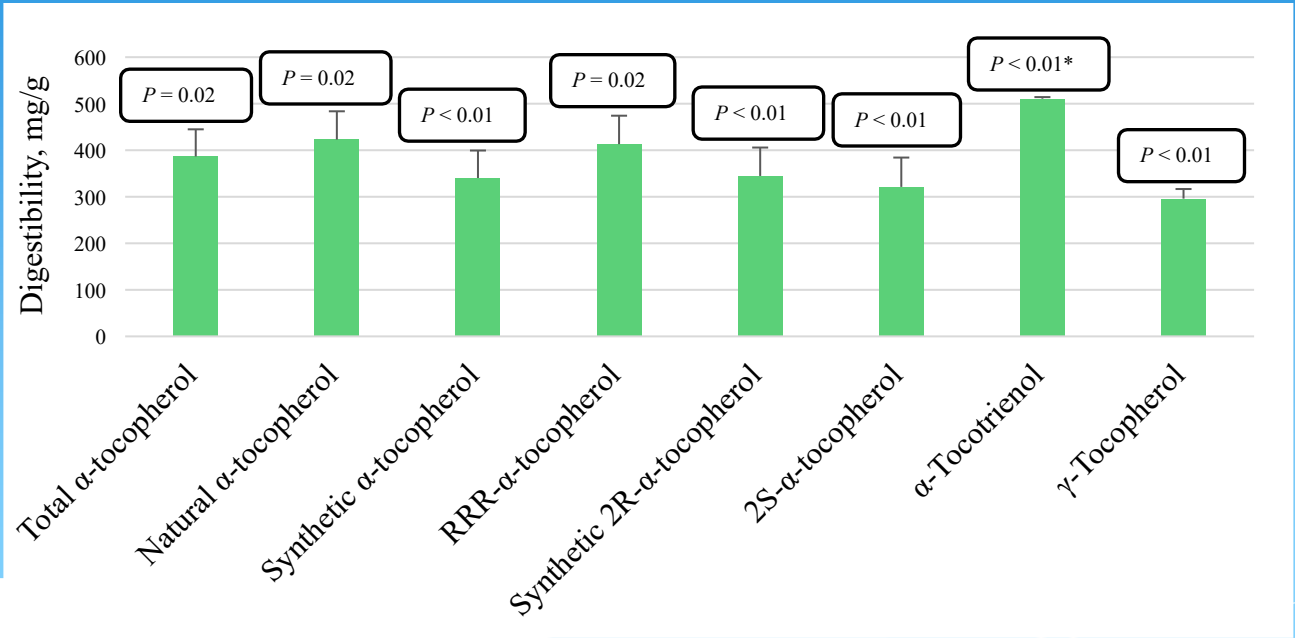
Digestibility of tocopherols, small intestine



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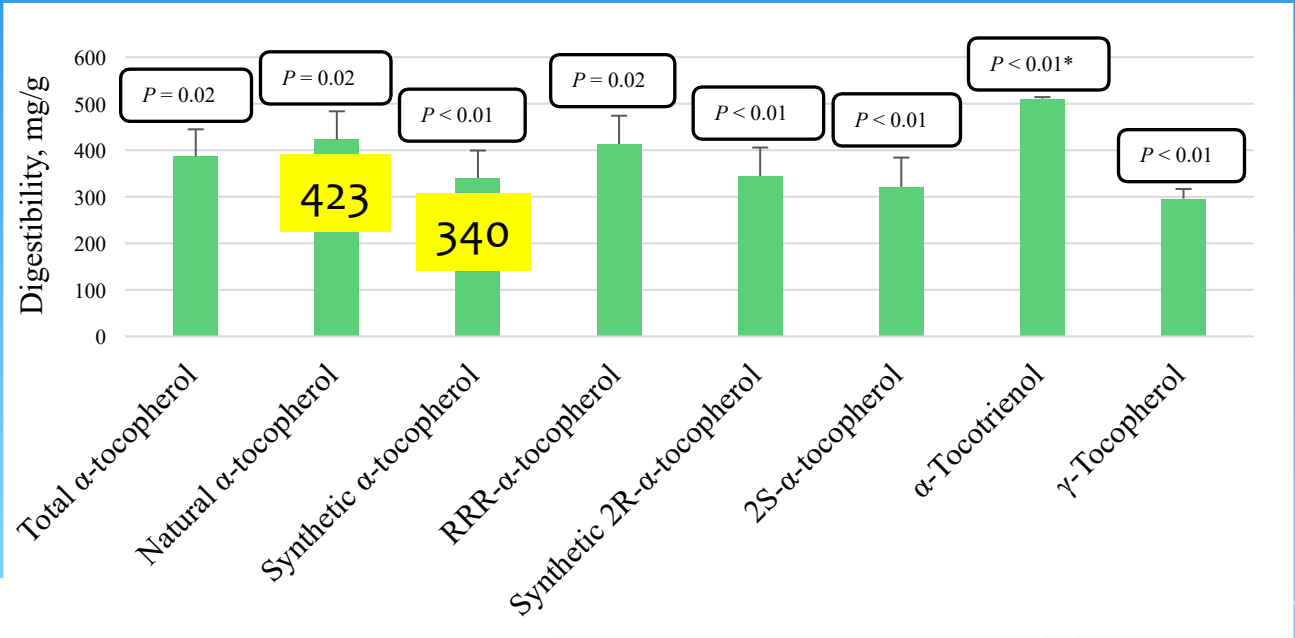

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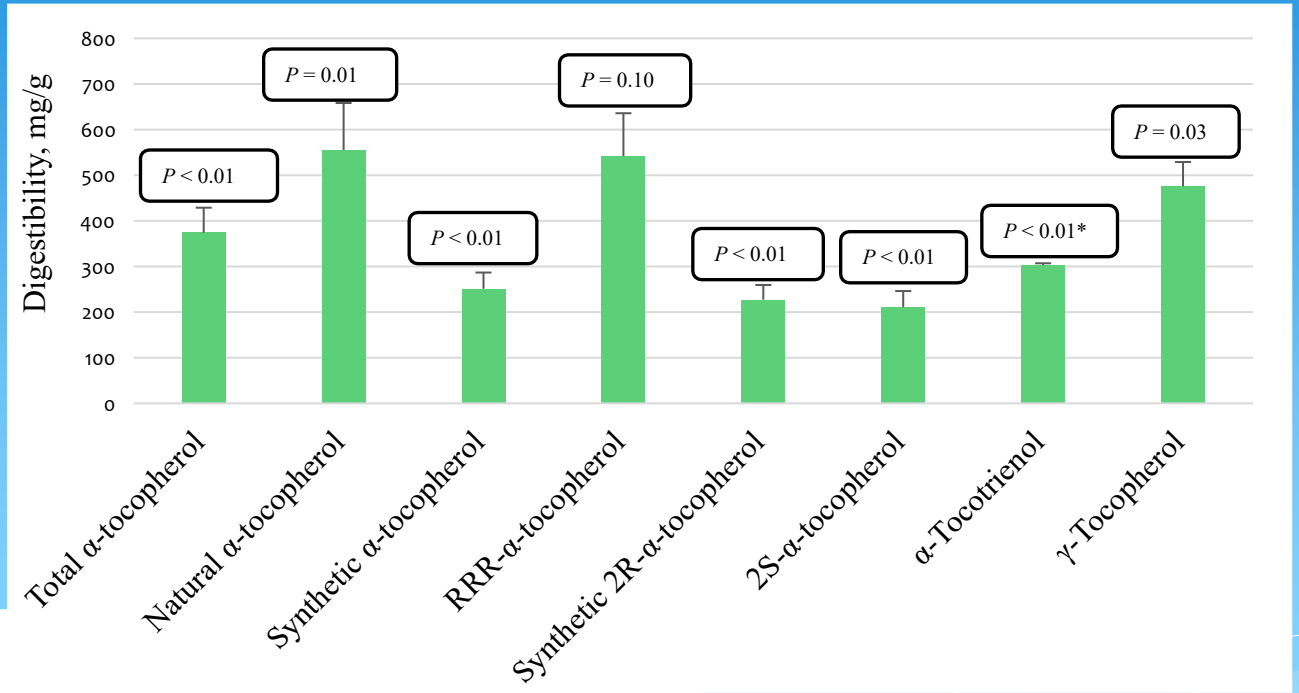
Digestibility of tocopherols, feed - ileum



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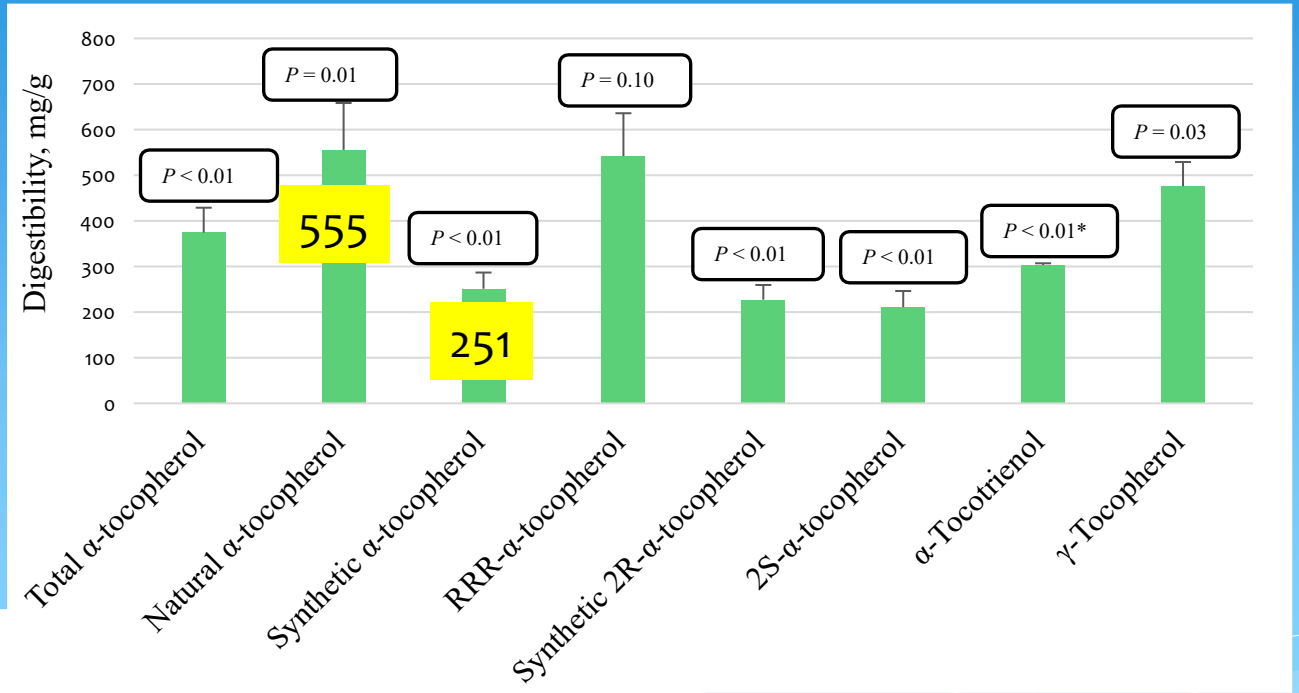

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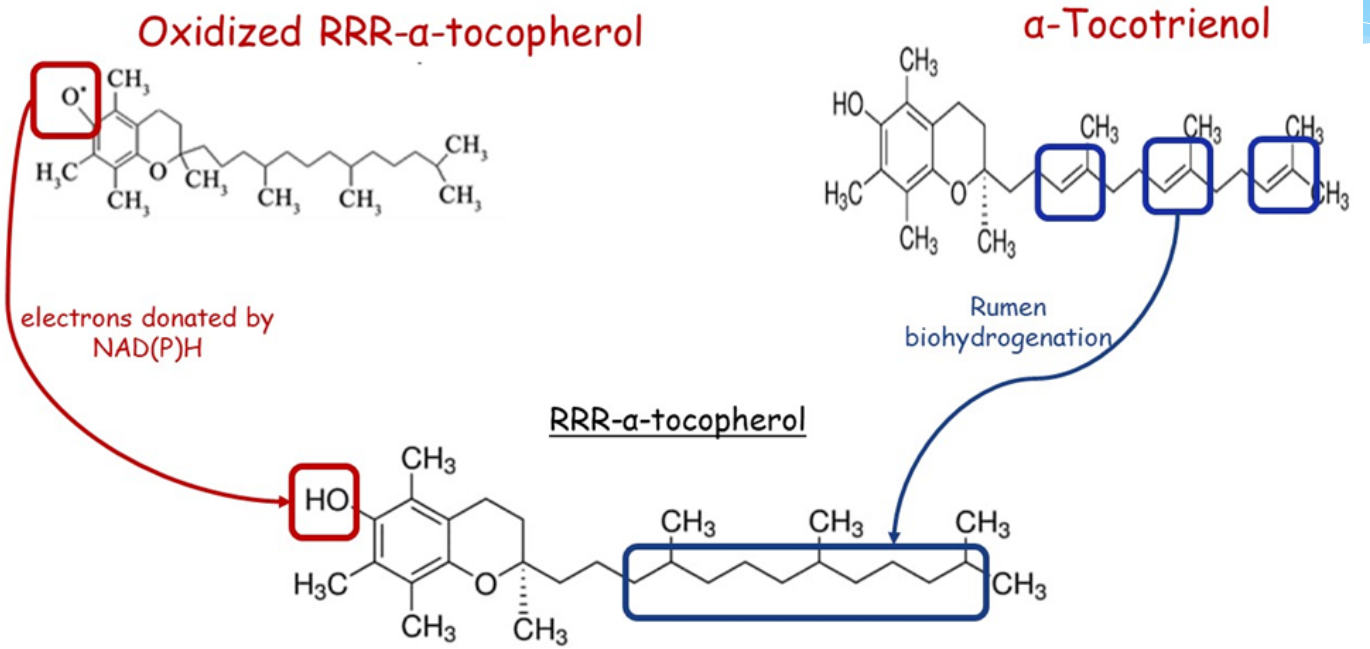
Posible ruminal formation of RRR-α-tocopherol

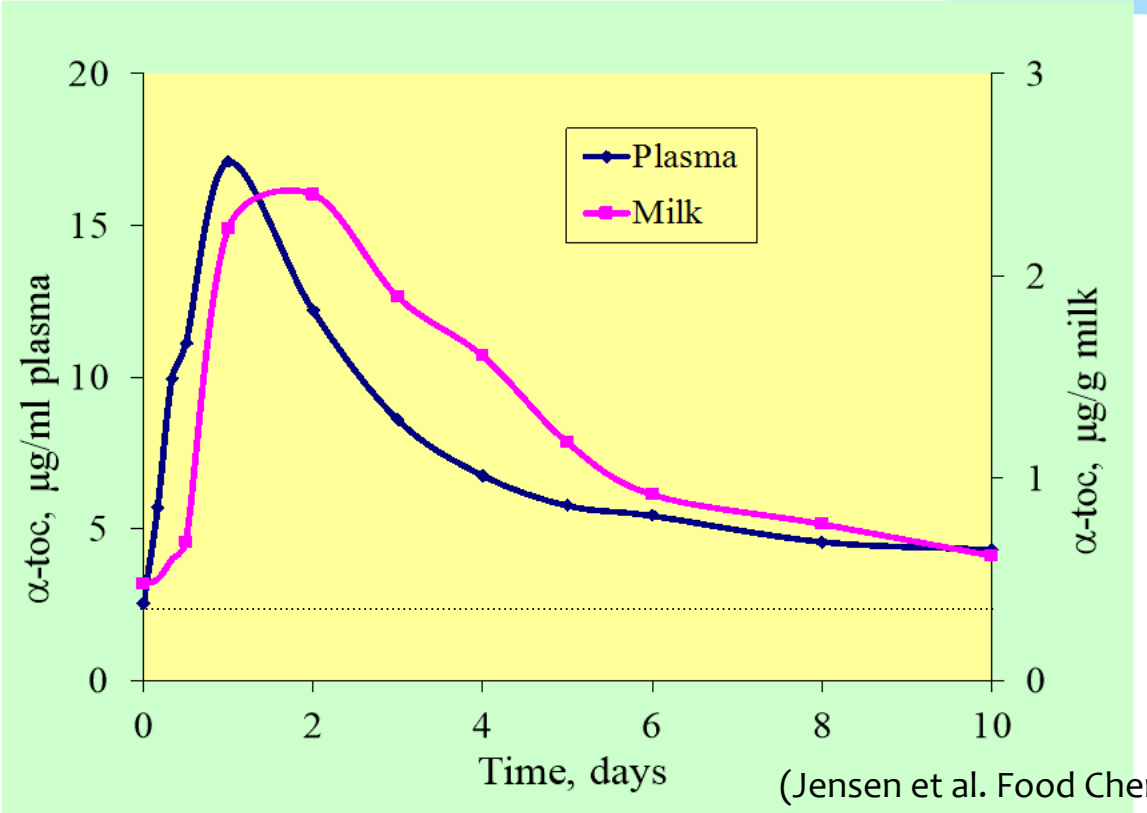


Second experiment
Pharmacokinetic studies of intramuscular injected *all-rac*-a-tocopherol in cows measured in blood and milk

- Intramuscular injection of 2.5 g *all-rac*-α-tocopheryl acetate into 4 lactating cows.
- Blood and milk samples through 10 days.
- Quantitative analysis of individual stereoisomers of α-tocopherol.

(Jensen et al. Food Chem 2020)

Total α-Tocopherol concentration in plasma and milk after i.m. injection of 2.5 g *all-rac*-α-tocopheryl acetate



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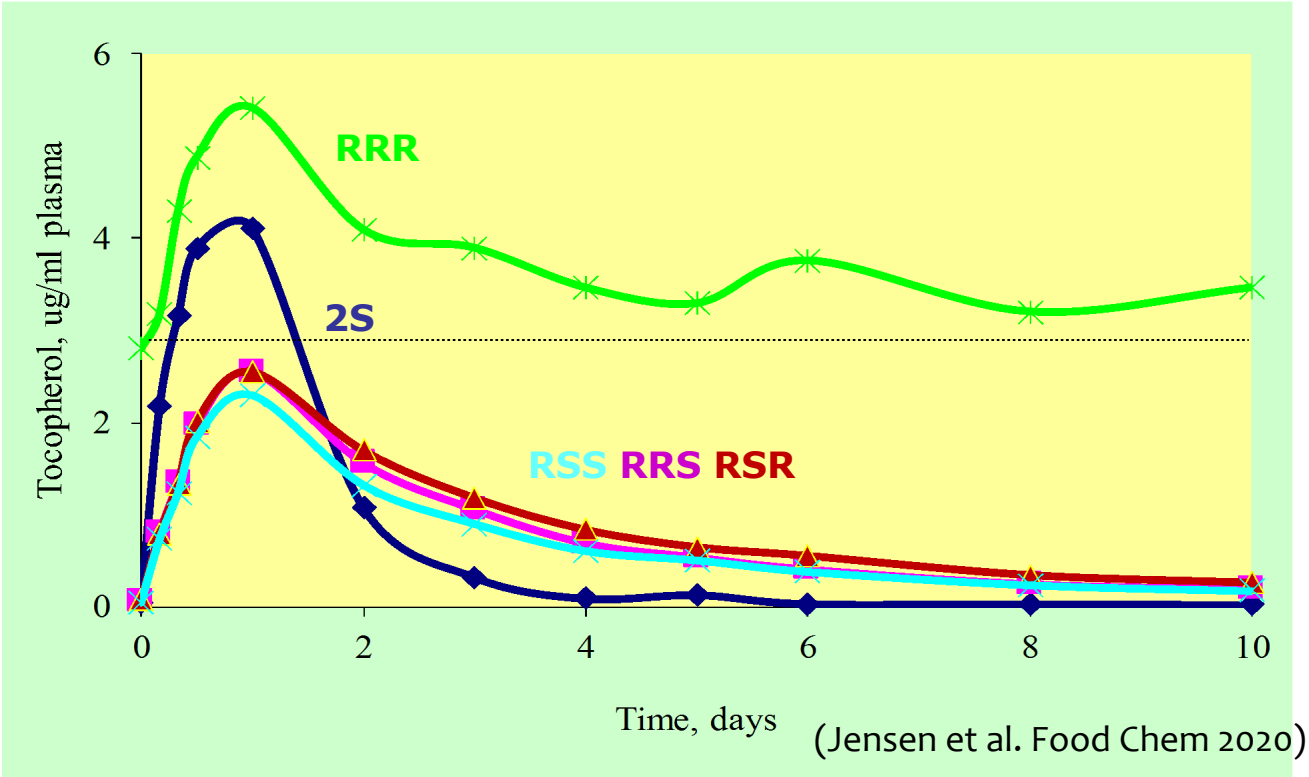
α-Tocopherol stereoisomers in plasma



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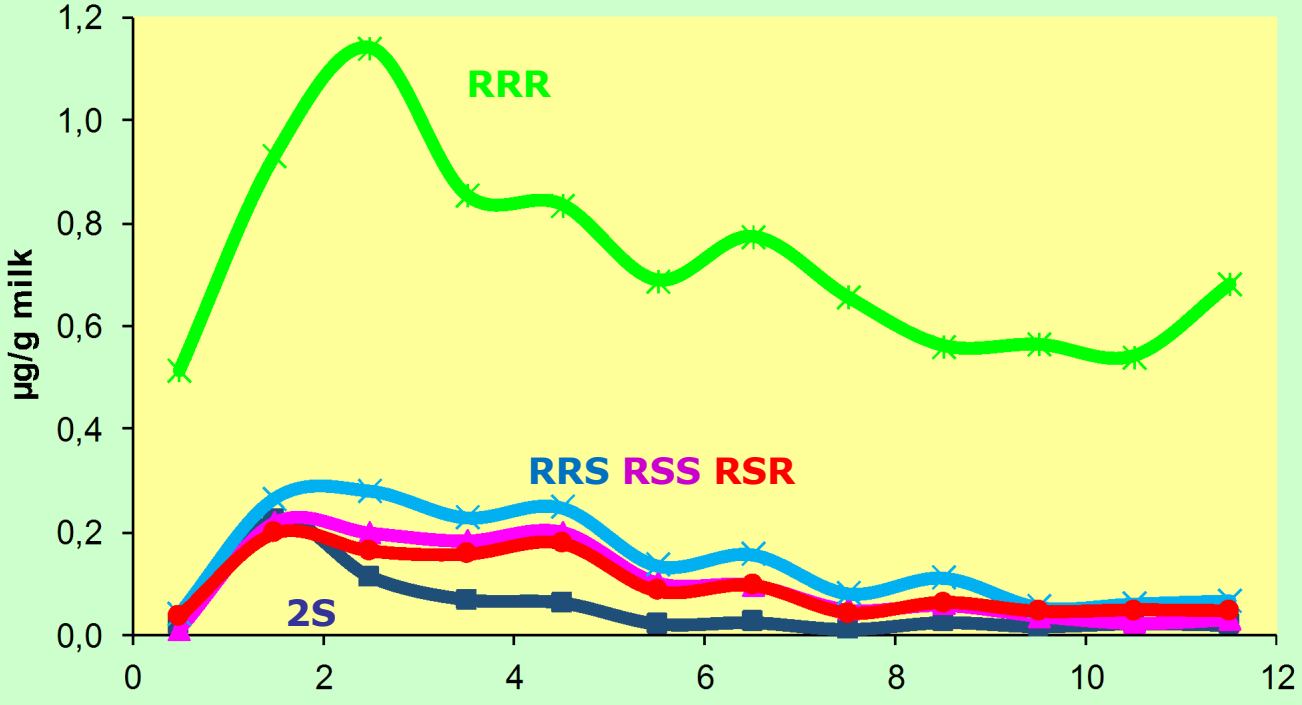
α-Tocopherol stereoisomers in milk



(Jensen et al. Food Chem 2020)

Half life ($t_{½}$) of α-tocopherol stereoisomers in plasma after i.m. injection of 2.5 g *all-rac*-α-tocopheryl acetate

	RRR	RRS RSS RSR	2S
Elimination rate, h	0.36^{b}	0.33^{b} 0.73^{b} 0.78^{b}	1.92^{a}
Half life $t_{½}$	2.92^{a}	0.53^{b} 0.95^{b} 0.95^{b}	0.38^{b}
Relative bioavailability compared to RRR-α-tocopherol	1.00^{a}	1.05^{a} 0.87^{a} 0.83^{a}	0.17^{b}

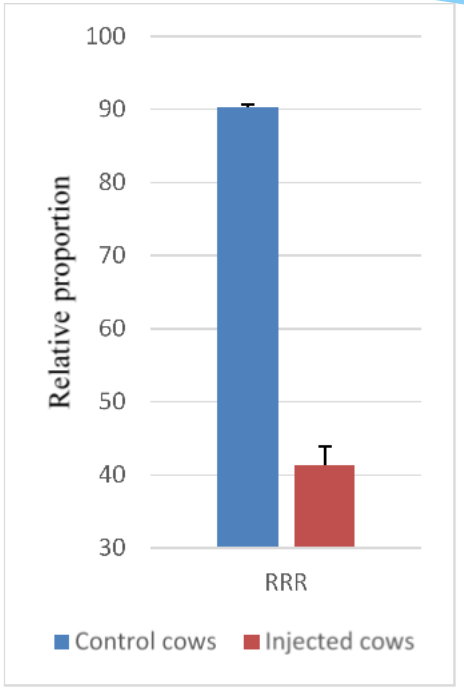
(Jensen et al. Food Chem 2020)

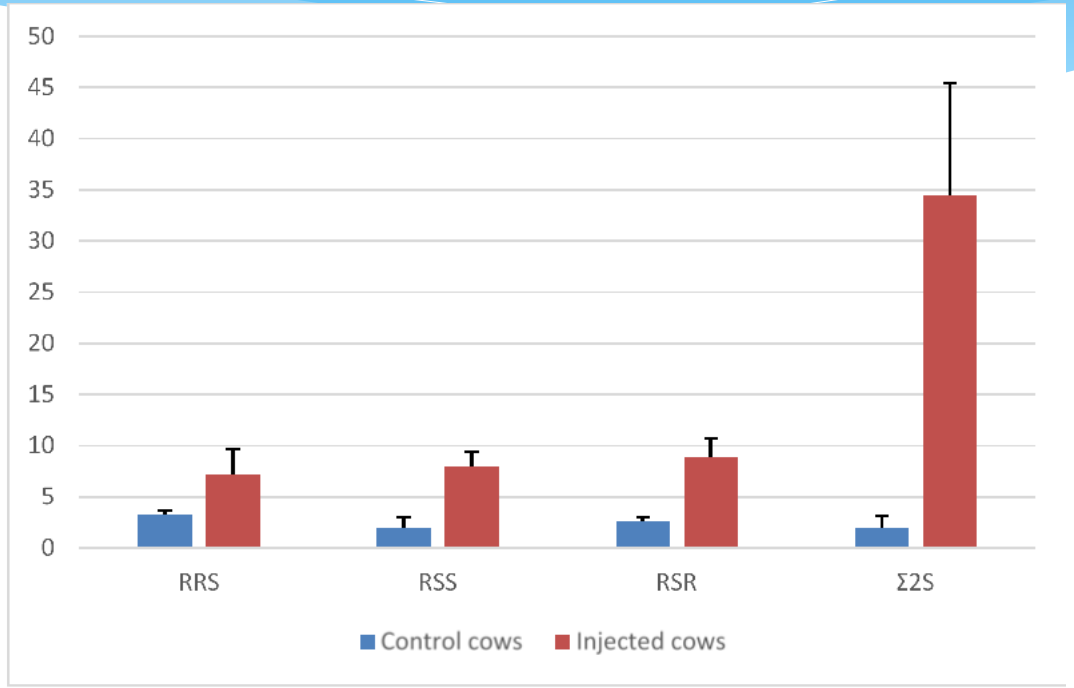
Accumulated secretion and relative secretion of α-tocopherol in milk after i.m. injection of 2.5 g *all-rac*-α-tocopheryl acetate

	RRR	RRS RSS RSR	2S
Accumulated secretion, mg	50.8^{a}	22.6^{b} 20.1^{b} 17.9^{b}	6.7^{c}
Total secretion of injected (%)	16.3^{a}	7.24^{b} 6.43^{b} 5.74^{b}	0.67^{c}
Relative bioavailability compared to RRR-α-tocopherol	1.00^{a}	0.51^{b} 0.46^{b} 0.39^{a}	0.05^{c}

(Jensen et al. Food Chem 2020)

Relative proportion of stereoisomers of α-tocopherol in liver from cows prior to and 36 h following injection of all-rac-α-tocopheryl acetate





(Jensen et al. Food Chem 2020)

Conclusions rumen balance and absorption of tocopherols by dairy cows

- Roughage is an important vitamin E source
- Degradation of tocopherols seems to take place in the rumen, but
- RRR-α-tocopherol is produced in the rumen
  (184 mg/day in the present experiment)
- RRR-α-tocotrienol and oxidized RRR-α-tocopherol may be the precursors
- Overall feed to ileum digestibility was measured to be
  251 mg/g for synthetic α-tocopherol
  555 mg/g for RRR-α-tocopherol

Conclusions, metabolism of α-tocopherols by dairy cows

- α-Tocopherol consist of 8 stereoisomers with different biological activity
- RRR-α-tocopherol is the primary tocopherol utilized by cows.
- Synthetic isomers shows the fastest elimination rate
- Shortest half life
- Lowest bioavailability
- 2S stereoisomers of α-tocopherols is almost completely absent in milk
- Liver accumulate 2S stereoisomers of α-tocopherols

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