

COMMON SUPPLEMENTS AND HERBS FOR CARDIOVASCULAR DISEASE

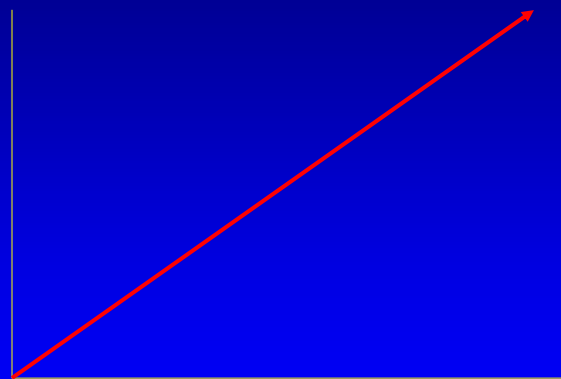


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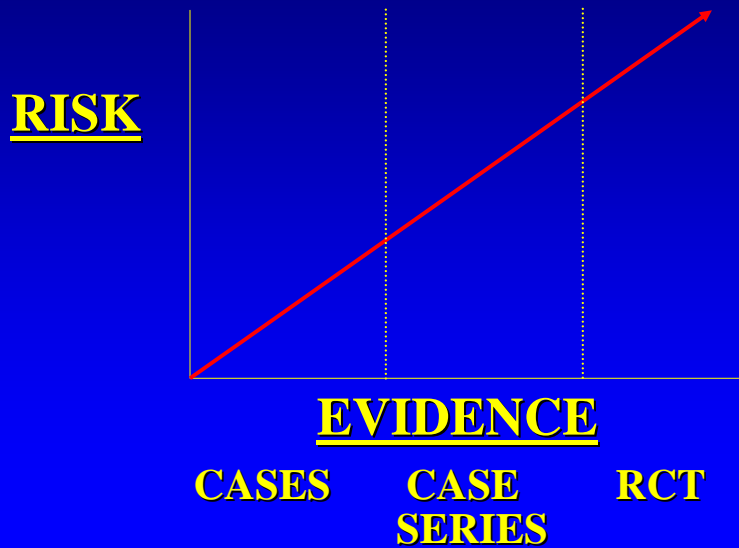
THRESHOLD FOR ACCEPTANCE

RISK



EVIDENCE

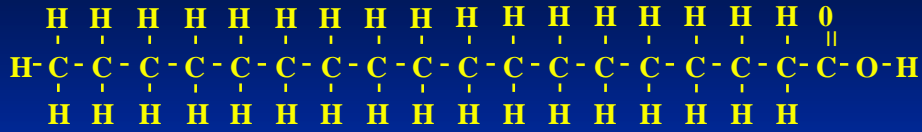
THRESHOLD FOR ACCEPTANCE



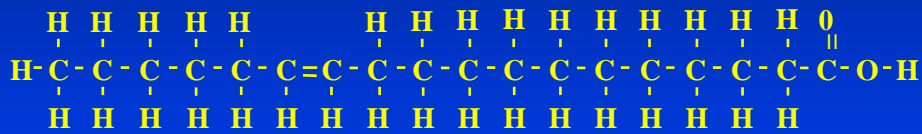
SUPPLEMENTS

- Omega-3 Fatty Acids (Fish oils)
- Mitochondrial Supplements
 - Coenzyme-Q10
 - D-Ribose
- Hawthorn (*Crataegus sp.*)
- Thrombolytics - Nattokinase

FATTY ACIDS

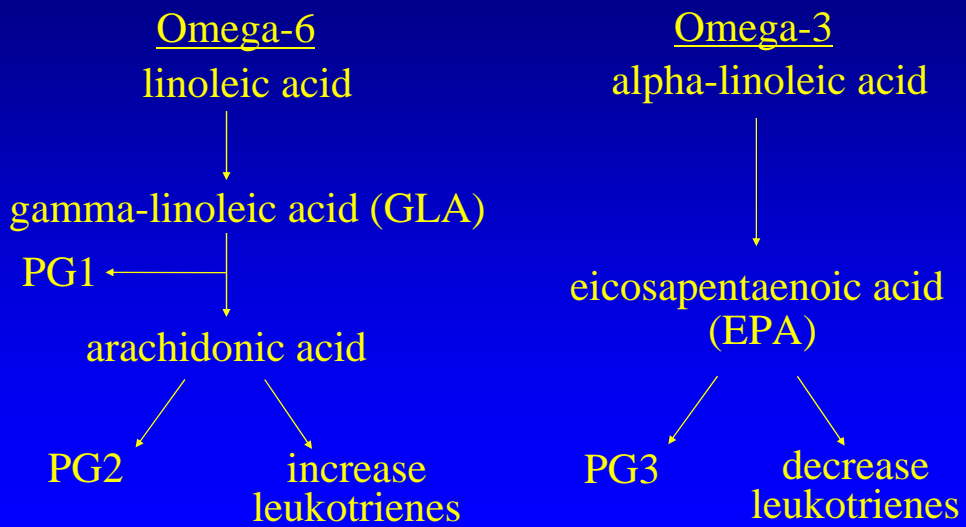


Saturated Fatty Acid



Omega-6 (linoleic acid)

ESSENTIAL FATTY ACIDS



OMEGA-3 FATTY ACIDS - POTENTIAL MECHANISMS

- ↓ Inflammation
 - ↓ Leukotrienes, ↓ NF- κ B, ↓ inflam. PG's
 - Lipoprotein lipase
- ↓ Coagulation / platelet aggregation
 - ↑ PG3, ↓ Thromboxane A₂
- ↓ Arrhythmias
 - ↓ Na⁺ (EPA/DHA) and K⁺ (DHA) channels
 - ↓ Thromboxane A₂
- ↓ Blood pressure

OMEGA-3 FATTY ACIDS - SECONDARY PREVENTION (I)

Mortality

	n	All cause	Cardiac	Sudden
GISSI (2002)	11,324	0.79 (.66-.93)	0.65 (.51-.82)	0.55 (.39-0.77)
Marik (2009) Systematic Review	39,044 (11 RCT)	0.92 (.85-.99)	0.87 (.79-.95)	0.87 (.76-.99)

OMEGA-3 FATTY ACIDS - SECONDARY PREVENTION (II)

- ICD - No effect (3 RCT)
 - Wang 2006 (Systematic Review)
 - Leon 2009 (BMJ meta-analysis)
- Arrhythmias - No effect
 - Leon 2009 (BMJ meta-analysis)

OMEGA-3 FATTY ACIDS - PRIMARY PREVENTION (I) EFA CONSUMPTION

..... Mortality

	All cause	Cardiac	Sudden	MI
PCT	+ 3/4	+ 1/2 (+ MRFIT)		+ 3/5 (+ NHS)
Case- Control				+ 1/1

(Wang - 2006 Am J Clin Nutr)

OMEGA-3 FATTY ACIDS - PRIMARY PREVENTION (II) FISH CONSUMPTION

..... Mortality

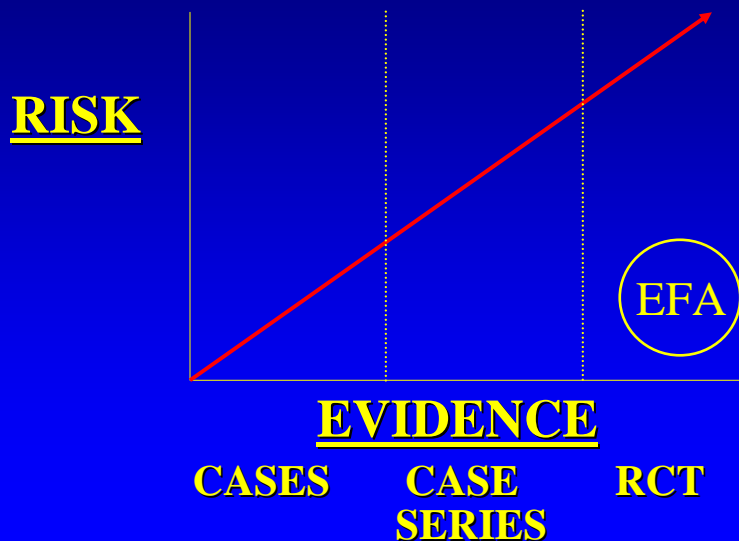
	All cause	Cardiac	Sudden	MI
PCT	+ 3/11 (+ PHS / NHS)	+ 4/15	+ 2/2 (+ PHS)	+ 4/9
Case- Control			+ 1/1	+ 1/4

(Wang - 2006 Am J Clin Nutr)

OMEGA-3 FATTY ACIDS - ADVERSE EFFECTS

- ↓ Coagulation / platelet aggregation
 - Esp. - > 3,000 mg/d
 - Labs - BT, Platelet Function Studies
- GI /Taste

THRESHOLD FOR ACCEPTANCE



ESSENTIAL FATTY ACIDS - RECOMMENDATIONS OMEGA 3 FISH OIL

- 1,000-3,000 mg/d
 - Esp. DHA (GISSI - 465 mg. EPA / 386 DHA)
- Concentrated DHA (200-250 mg. DHA)
 - Nordic Naturals - Ultimate Omega
 - Carlson - Super Omega
- Non-concentrated (120-150 mg. DHA)
 - Trader Joe's - Omega 3

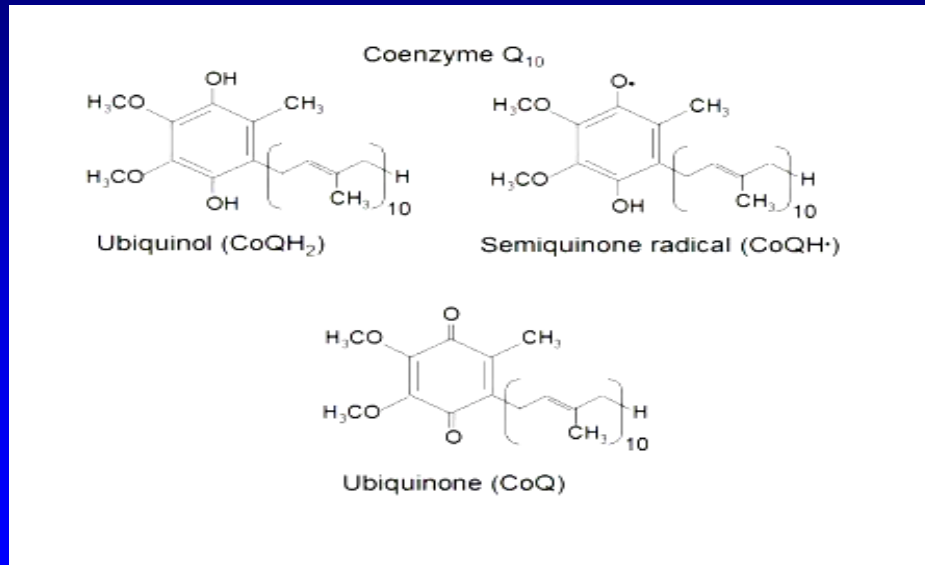
MITOCHONDRIAL SUPPLEMENTS

- Coenzyme-Q10
- D-Ribose
- (NADH, glutathione, carnitine, malate, alpha-lipoic acid ...)

COENZYME-Q10

- Anti-oxidant (Ubiquinone → Ubiquinol)
- Mitochondrial Redox (Complexes I, II, III)

FORMS OF COENZYME-Q10



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COENZYME-Q10

- Total body content - 0.5-1.5 gm
 - Decrease with age & chronic disease
- Avg. US diet - 5 mg/d
 - Diet examples - 30 mg CoQ10
 - 1 # sardines
 - 2 # beef
 - 2 1/2 # peanuts
 - 20 oz. spinach

COENZYME-Q10

- CHF
 - Langsjoen 1999 - Review 34 RCT
 - Mortensen 2003 - Review 13 RCT (n=988)
 - ↓ - Sx
 - ↑ - exercise tol, QOL, cardiac function
- HTN
 - Mortensen 2003 - Review 3 Open / 4 RCT
 - Open - ↓ SBP/DBP - 15-20 / 8-15 mm Hg
 - RCT - ↓ SBP/DBP - 11-19 / 2-16 mm Hg
 - ↓ Medications (50% dec ▪ ≥ 1 medication)

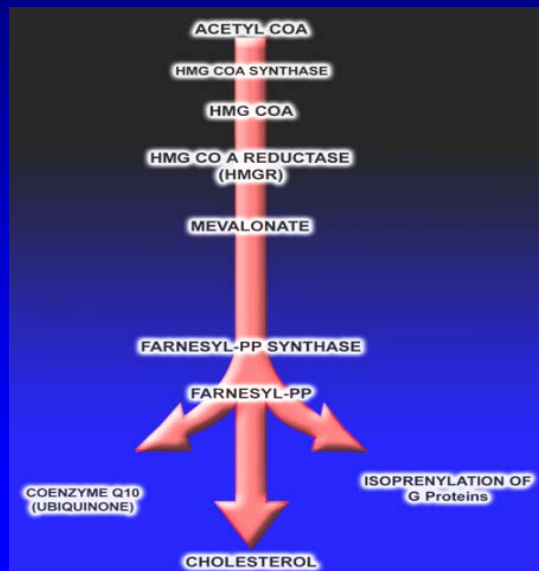
COENZYME-Q10

- MI
 - Mortensen 2003 - Review 2 RCT
 - Singh 1998 (Cardiovasc Drugs Ther) n=71
 - ↓ - angina, arrhythmias, cardiac death, secondary MI,
 - ↑ - LV function
- Open Heart Surgery / CABG / Valve
 - ↓ - Pump times , recovery times

COENZYME-Q10 - ADVERSE EFFECTS / INTERACTIONS

- Decreased by:
 - HMG-CoA Reductase Inhibitors
 - Oral hypoglycemics (e.g. gemfibrozil)
 - Adriamycin
 - β - Blockers
- Antagonizes:
 - Coumadin/Warfarin (\downarrow INR)

COENZYME-Q10 AND STATINS

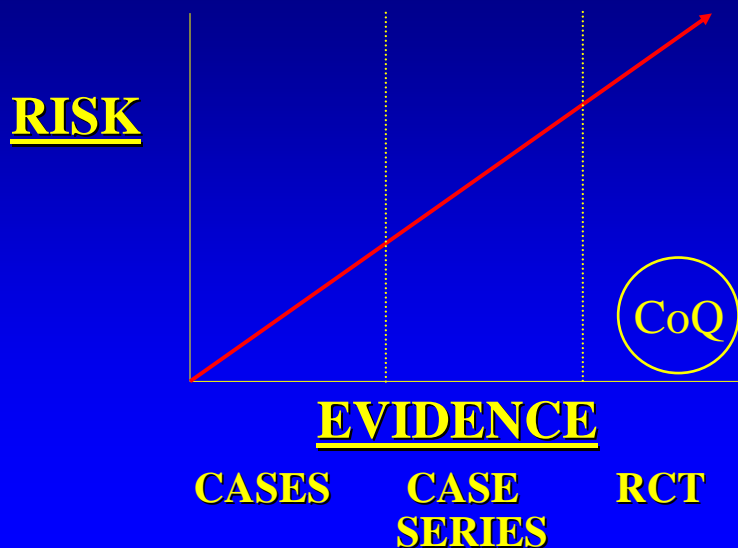


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COENZYME-Q10 AND STATINS

- Reviews:
 - Schaars CF. Curr Opin Lipidol 2008;19;553-7.
 - Marcoff L. J Am Coll Cardiol 2007;49;2231-7.
- Conclusions:
 - Statins - ↓ CoQ10 blood levels - 20-35%
 - Effect on intramuscular levels/clinical - ?
 - Effect of supplementation - Mixed (1+/2 - RCT)

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COENZYME-Q10 - RECOMMENDATIONS

- 60-200 mg/d (up to 2,000 mg)
 - ? Increase on Statin Rx
 - Preparations
 - Trans > Cis
 - Oil > powder
- Brands
 - Vitaline - Integrative Therapeutics
 - Jarrow

D-RIBOSE

QuickTime™ and a
decompressor
are needed to see this picture.

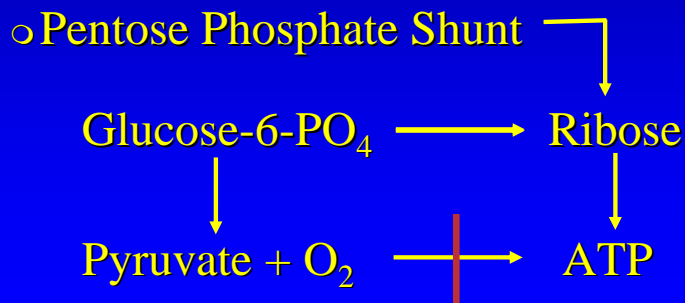
- **Not free-form in diet - synthesized in body**
- **L- isomer - no biological activity**

D-RIBOSE

- Purine synthesis (DNA / RNA / AMP / ATP)
- Mitochondria / Energy
 - ATP = ribose + adenine + PO_4
 - FAD = ribose + adenine + riboflavin
 - Acetyl CoA = ribose + adenine + pantothenic acid

D-RIBOSE - POTENTIAL MECHANISMS

- Rebuild purines (AMP / ATP)
- Energy substrate



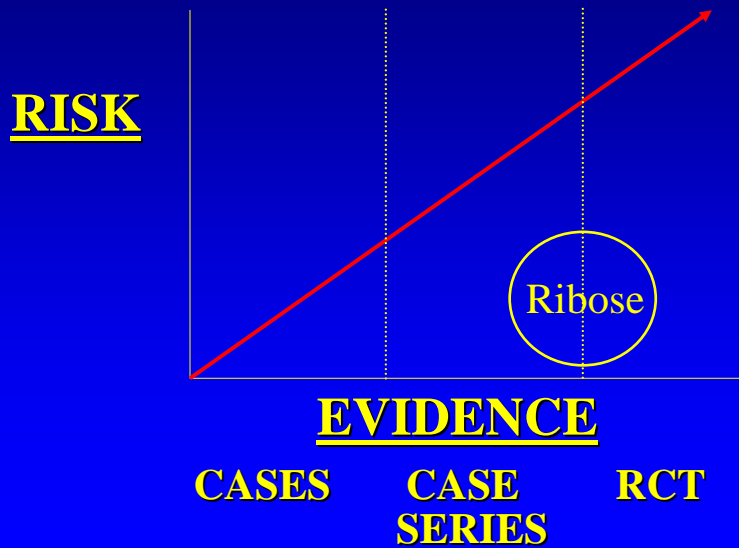
D-RIBOSE

- Animal Studies - Ischemia / Pump run
- Recovery after Pump run
 - Perkowski 2005 (n = 44) ↑ 44% cardiac indices
- Energy / performance - Bodybuilders, training, etc.
- CAD - ↑ Stress / Treadmill Test
 - Perlmutter 1991 (n =17)
 - Pliml 1992 (n = 20)

D-RIBOSE - CHF

	n	NYHA	Outcomes
Illien 2001	12	II-III	↑ - SVI, EF, AC, LVVs
Omran 2001	15	II-III	↑ - AC, QOL, phys function
Sharma 2005	15	II-III	↑ - MPI, VO ₂ max, VE
Vijay 2005	15	III-IV	↑ - VO ₂ max, VE, SV (O ₂ pulse)

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D-RIBOSE - RECOMMENDATIONS

- 5 mg tid (max 60 mg/d)
- Brands:
 - Corvalen - Integrative Therapeutics
 - Corvalen-M (with malate)

HAWTHORN (*Crataegus sp.*)

- Species (> 280)
 - *C. laevigata*
(*C. oxyacantha*)
 - *C. monogyna*
- Preparations
 - Leaf and Flower

HAWTHORN

- Active constituents
 - Flavonoids - 0.5 - 1.8%
 - Procyanidins
 - Oligomeric (1.0-2.4%) > Polymeric
- Standardized Preparation
 - WS1442 - 80 mg flower, fruit, & leaf,
18.8% (15 mg) oligomeric procyanidins

HAWTHORN - POTENTIAL MECHANISMS

- ACE-inhibitor - Vasodilator, ↓ BP
- Inotropic
 - Glycoside-like (cAMP independent)
 - Possible phosphodiesterase inhib (↑ cAMP)
- Anti-arrhythmic
 - Blocks Na⁺ / K⁺ ATPase (Class III-like)

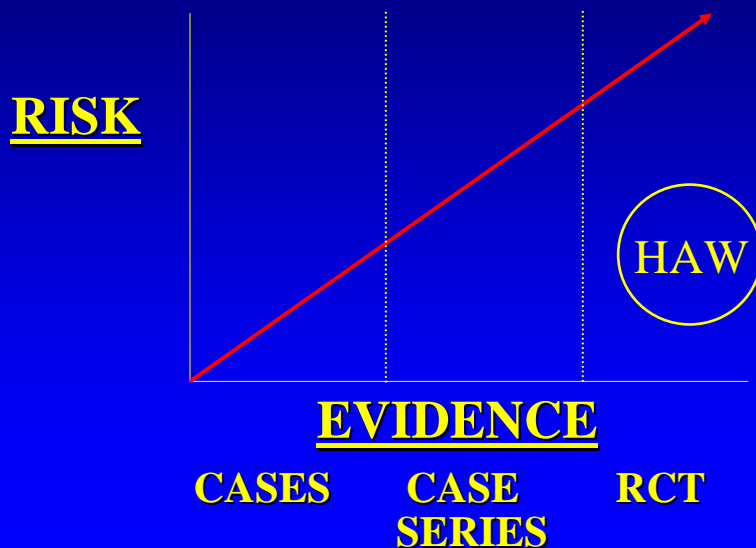
HAWTHORN - CHF REVIEWS / META-ANAYSES

	n (studies)	NYHA	Max. Work	Pressure X HR	Sx
Pittler 2003	632 (8)	I-II	+ (↑ 7 Watt)	+	+ (↓dyspnea & fatigue)
Guo 2008	855 (10)	I-II	+ (↑ 5.4 Watt)	+	+ (↓dyspnea & fatigue)

HAWTHORN - ADVERSE EFFECTS

- Occ. - nausea, GI Sx, dizziness
- ↓ BP
- Drug interactions - theoretical
 - May potentiate coronary artery dilation
 - Theophylline, caffeine, sodium nitrate, adenosine, epinephrine
 - No potentiation - digoxin

THRESHOLD FOR ACCEPTANCE



HAWTHORN - RECOMMENDATIONS

- NYHA I-II
- 160 - 900 mg/d (WS 1442)
 - CardioMax® WS 1442® - 450 mg

THROMBOLYTICS

- Nattokinase
 - Natto - *B. subtilis* / *natto* + boiled soybeans
 - 275 AA, serine peptidase, PO & IV
 - Direct - plasmin-like, ACE inhibitor
 - Indirect - stimulate plasmin, urokinase
- Serrapeptidase - silkworm
- Lumbrokinase / Buoloke - earthworm

NATTOKINASE (I)

- Animal studies
- HTN - Kim 2008 (n=73)
 - ↓ SBP -5.6 mm Hg (-10.5 to -0.6)
 - ↓ DBP -2.8 mm Hg (-5.3 to -0.3)

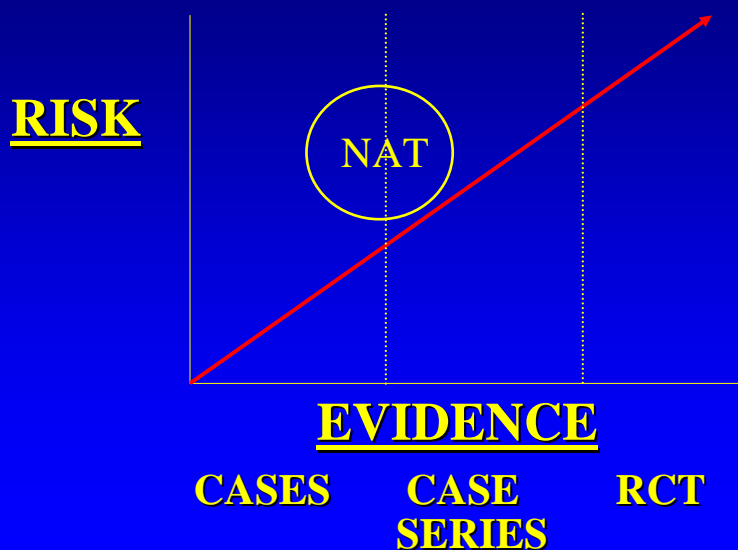
NATTOKINASE (II) - CLOTTING

- Sumi 1990 - (n=12) ↑ thrombolysis 48%
- Hsia 2009 - Healthy / dialysis / CAD
 - ↓ Fibrinogen (7-10%), VII (7-14%),
VIII (17-19%)
- Cesarone 2003 - LONG-FLITE (n=186)
 - Control - 7 clots, Natto - 0 clots

NATTOKINASE - ADVERSE EFFECTS

- Chang 2008 - Case Report
 - Prior CVA, ASA prophylaxis
 - CVA after Nattokinase (400 mg/d x7d)
- Not a substitute for Coumadin / Warfarin

THRESHOLD FOR ACCEPTANCE



OMEGA-3 FATTY ACIDS - REFS REVIEWS/META-ANALYSES

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- Marik PE. Clin Cardiol 2009:32;365-72.

COENZYME-Q10 - REFS REVIEWS/META-ANALYSES

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RIBOSE - REFS

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HAWTHORN (*Crataegus sp.*) - REFS REVIEWS/META-ANALYSES

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NATTOKINASE - REFS

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COENZYME-Q10 - GENETICS

- NAD(P)H:quinone oxidoreductase (NQO1)
 - C609T SNP - 30-50% of population
 - ↓ Conversion - Ubiquinone → Ubiquinol
(supplement) (active)
- Blood levels/ ratios - ubiquinol/ubiquinone
- New Ubiquinol supplement
 - UBQH - Integrative Therapeutics