Table 3-1. Summary of Study Design and Outcomes Evaluated in Whole Animal Studies (23 feeding and 3 infusion studies) *

Author, Year	Omega-3 Arm(s)	Control Arm*	Animals	Outcomes Evaluated							
				VF	VT	VPB	AS	Deaths	IS	TSR	VFT
Feeding studies:											
Omega-3 PUFAs vs Omega-6 PUFAs											
Abeywardena, 1995	Soybean, MaxEPA™	SSO	Rats	v	v	v	v	v			
Anderson, 1996	MaxEPA™	Safflower	Rats	v	v	v	v				
Charnock, 1992	Fish oil	SSO	Monkeys	v							v
Charnock, 1991	Fish oil	SSO	Rats	v	v	v	v				
Hock, 1990	Menhaden	Corn	Rats	v			v	v			
Hock, 1987	Menhaden	Corn	Rats			v		v			
Isensee, 1994	Linseed, Fish oil	Corn	Rats	v	v				v	v	
McLennan, 1995	Canola, Soybean	SSO	Rats	v	v	v	v	v			
McLennan, 1992	Tuna	SSO	Monkeys	v							v
McLennan, 1993	Fish oil	SSO	Rats	v	v	v	v	v		v	
McLennan, 1990	Tuna	SSO	Rats	v	v	v	v	v		v	
McLennan, 1988	Tuna	SSO	Rats	v	v		v	v	v		
McLennan, Bridle, 1993	Fish oil	SSO	Monkeys	v							v
Omega-3 PUFAs vs MUFAs											
McLennan, 1996	EPA-e, DHA-e, EPA-e+DHA-e	Olive	Rats	v			v				
Omega-3 PUFAs vs SFAs											
al Makdessi, 1995	Sardine	Coconut	Rats						v	v	
Chen, 1994	Fish oil	Coconut	Rabbits			v		v			
Hartog, 1987	Mackerel	Lard	Piglets	v	v	v		v			
Pepe, 1996	Fish oil	Sheep fat	Rats	v	v	v					v
Yang, 1993	Fish oil	Butter	Rats	v	v						
Omega-3 PUFAs vs Chows											
Culp, 1980	Menhaden	Friskies Dinner	Dogs			v		v	v		
Kinoshita, 1994	EPA-e	Oriental Yeast Co.	Dogs	v	v	v	v				
Oskarsson, 1993	MaxEPA™	Chows	Dogs						v		
Otsuji, 1993	EPA-e	Oriental Yeast Co.	Dogs					v	v	v	
	Total =			**17**	**12**	**12**	**10**	**11**	**6**	**5**	**4**
Infusion studies:											
Omega-3 PUFAs vs Omega-6 PUFAs											
Billman, 1999	Albumin-bound ALA, EPA, DHA	Soybean or saline	Dogs	v							
Billman, 1994	Fish oil emulsion	Soybean	Dogs	v							
Omega-3 PUFAs vs Chows											
Lo, 1991	ALA	Buffer	Dogs		v	v					
	Total =			**2**	**1**	**1**					

SSO = sunflower seed oil; VF=ventricular fibrillation; VT=ventricular tachycardia; VPB=ventricular premature beats; AS=arrhythmia score; IS=infarct size; VFT=ventricular fibrillation threshold, measured only in VF inducible animals; TSR =length of time in normal sinus rhythm; EPA-e = EPA esters; DHA-e = DHA esters

* For the purposes of our evidence review, only optimal comparison group was chosen. See Chapter 2: Methods.

Table 3-2. Summary Of Study Design And Outcomes Evaluated In Whole Animal/Isolated Organ And Cell Studies

Author	Species	Stage	Sex	Omega-3	Ctrl	Omega-3	Omega-3	ICU	ICH	IPIM	BEP	CP
Croset, 1989a	Mouse	W	M	STD+DHA-DOSE	STD					v		
Croset, 1989b	Mouse	W	M	ALAe	OO+SAF	EPAe	DHAe			v		
Benediktsdottir, 1988	Rat	A	M	CLO	CO					v		
Demaison, 1993	Rat	W	M	LIN	SF							v
Karmazyn, 1987	Rat	W	M+F	STD+CLO	STD					v	v	
Laustiola, 1986	Rat	W	M	STD+CLO	STD							v
Leifert, 2000	Rat	YA	M	FO	LARD			v				v
Minarovic, 1997	Rat	YA	M	FO	HF			v	v			
Taffet, 1993	Rat	YA	F	CO+MenO	CO					v		
Maixent, 1999	Rat	A	M	STD+FO	STD					v		
Chen, 1994	Rabbit	A	M	HC+FO	HC					v		
Heard, 1992	Rat	A	M	SAF+MenO	SAF							v
Gudmundsdottir, 1991	Rat	A,O	M	CLO	CO			v				
Reig, 1993	Rat	YA	M	HF+FO	HF						v	v
Ku, 1997	Rat	O	F	HC+EPA	HC	HC+DHA						v
Honen, 2002	Rat	A	M	FO	RO					v		
Leifert, 2001	Rat	A	M	FO	SF					v		v
Pepe, 1999	Rat	A,O	M	FO	N-6					v		
Swanson, 1989	Mouse	W	M	SAF+MenO	SAF+CO					v		
Gillis, 1992	Rabbit	W	ND	FO	SAF						v	
Kinoshita, 1994	Dog	A	ND	STD+EPAe	STF					v		
								3	**1**	**12**	**3**	**7**

ICU=ion currents; ICH=ion channels; IPIM=ion pumps and ion channels; BEP=basal electromechanical parameters; CP=contractile parameters.

A=Adult
ALAe= Esterified alpha linoleic acid
CLO=cod liver oil
CO=corn oil
EPAe= Esterified eicosapentaenoic acid
FO=fish oil
HC=high cholesterol
HF=high fat
LIN=linseed oil
MenO= menhaden oil
N-6=nOmega-6 fatty acid
O= old
OO=olive oil
RO= rapeseed or canola oil
SAF=safflower oil
SF=saturated fat
STD=standard chow
W= weanling
YA=Young adult

Table 3-3. Summary of Study Design and Outcomes Evaluated in Isolated Organ and Cell Studies

Author	Species	Stage*	ICU	ICH	IPIM	BEP	CP
Bogdanov, 1998	Rat	Adult	v			v	
Courtois, 1992	Rat	W					v
De Jonge, 1996	Rat	W					v
Hallaq, 1990	Rat	W			v		v
Hallaq, 1992	Rat	W		v	v		v
Honore, 1994	Mouse	W	v	v			
Jahangiri, 2000	Rat	Adult					v
Kang, 1994	Rat	W					v
Juan, 1987	Guinea pig	Adult					v
Xiao, 2002	Ferret	Adult	v				
Kang, 1996	Rat	W			v		v
Leifert, 1999	Rat	Adult	v				
Leifert, 2000	Rat	Adult					v
Rodrigo, 1999	Rat, guinea pig	ND	v				v
MacLeod, 1998	Rat, guinea pig	Adult	v				v
O'Neill, 2002	Rat	Not sure	v		v		
Durot, 1997	Rat	W				v	v
Grynberg, 1988	Rat	W				v	v
Kang, 1995a	Rat	W				v	
Kang, 1997	Rat	W		v			
Li, 1997	Rat	W					v
Negretti, 2000	Rat	ND	v		v		v
Pepe, 1994	Rat	2-3 mo	v		v		v
Phillipson, 1985	Dog	ND			v		
Phillipson, 1987	Dog	ND			v		
Grynberg, 1996	Rat	W				v	v
Kang, 1995b	Rat	W					v
Fournier, 1995	Rat	W				v	v
Grynberg, 1995	Rat	W					v
Ferrier, 2002	Guinea pig	Adult	v				v
Reithman, 1996	Rats	W				v	v
Ponsard, 1999	Rats	W					v
Xiao, 1997	Rats	Adult	v		v		
Xiao, 1995	Rats	W	v				
Goel, 2002	Pig	Adult			v		
Vitelli, 2002	Rats	Adult			v		
Weylandt,1996	Rats	W				v	
Rinaldi, 2002	Rats	Adult			v	v	
Bayer, 1979	Cat	Adult				v	
Total			12	3	12	10	23

ICU=ion currents; ICH=ion channels; IPIM=ion pumps and ion channel movement ; BEP=basal electromechanical parameters; CP=contractile parameters.

*Stage: ND=no data; W = weanling

Table 3-4. Total Deaths in Ischemia-Reperfusion-Induced Arrhythmia: Comparison of Rats Fed Omega-3 Fatty Acids With Controls Fed Omega-6 PUFA Oils

Author, Year	Omega-3 Arms	Dosage, g/100 g	Duration	Omega-3 Fatty Acids		Control		RR (95% CI)	Experiment Protocols
				Event	Total	Event	Total		
ALA Oils									
Abeywardena, 1995	Soybean	0.4	9 months	2	18	1	18	2.0 (1.5-20)	5-min ischemia; 10-min reperfusion
McLennan, 1995	Soybean	1.1	5 weeks	3	10	2	10	1.5 (0.32-7.1)	5-min ischemia; reperfusion
								1.3 (0.25-6.8)	
McLennan, 1995	Soybean	1.1	5 weeks	2 *	13	2 †	14	0.20 (0.01-3.7)	15-min ischemia; reperfusion
								1.3 (0.25-6.8)	
McLennan, 1995	Canola	1.2	5 weeks	0	10	2	10	0.20 (0.01-3.7)	5-min ischemia; reperfusion
McLennan, 1995	Canola	1.2	5 weeks	3 ‡	16	2 †	14	1.1 (0.18-6.6)	15-min ischemia; reperfusion
	Meta-analysis: Total subjects = 133			**10**	**67**	**9**	**66**	**1.2 (0.51-2.6)**	**Random-effect model**
Fish Oils (EPA+DHA)									
Hock, 1987	Menhaden	1.0	4 weeks	2 ‡	13	2 ‡	14	1.1 (0.18-6.6)	15-min after ischemia without reperfusion
Hock, 1990	Menhaden	1.0	4 weeks	5	21	13	22	0.40 (0.17-0.93)	15-min ischemia; 24 h reperfusion
McLennan, 1993	Fish oil	2.6	12 weeks	0	10	1 *	12	0.39 (0.02-8.7)	5-min ischemia; 5-min reperfusion
McLennan, 1993	Fish oil	2.6	12 weeks	0	14	1 *	13	0.31 (0.01-7.0)	15-min ischemia; 5-min reperfusion
Abeywardena, 1995	MaxEPA™	3.3	9 months	0	18	1	18	0.33 (0.01-7.7)	5-min ischemia; 10-min reperfusion
McLennan, 1988	Tuna	3.7	12 months	0	10	0	10	1.0 (0.02-46)	15-min ischemia; reperfusion
McLennan, 1990	Tuna	3.7	18 months	0	7	0	7	1.0 (0.02-45)	15-min ischemia; reperfusion
	Meta-analysis: Total subjects = 169			**7**	**83**	**18**	**86**	**0.47 (0.23-0.93)**	**Random-effect model**

RR = risk ratio = (omega-3 FA event rate)/(control's event rate)

* All deaths occurred during ischemia procedure

† One death occurred during ischemia procedure

‡ Deaths were observed 15-min after ischemia procedure without reperfusion

Figure 3-1. Total deaths in ischemia-reperfusion-induced arrhythmia: comparison of rats fed, alpha linolenic acid (ALA) with controls fed omega-6 PUFA oils

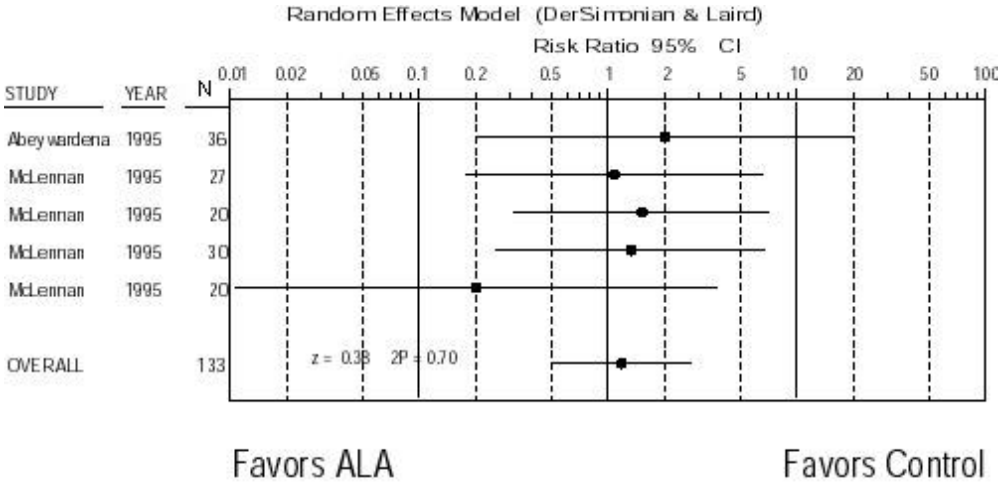

Figure 3-2. Total deaths in ischemia-reperfusion-induced arrhythmia: comparison of rats fed fish oils with controls fed omega-6 PUFA oils

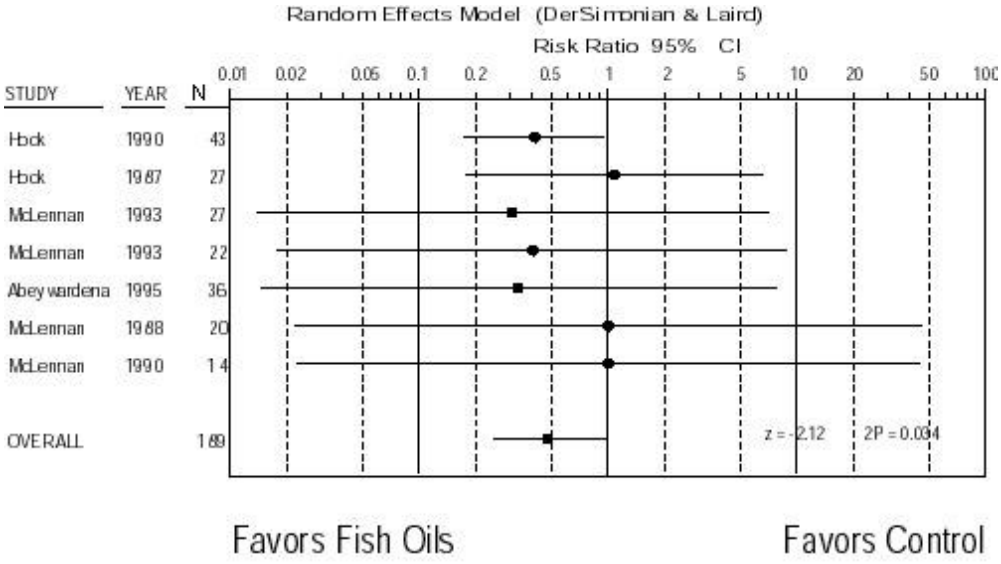

Table 3-5. Sensitivity Analysis on Total Deaths In Ischemia-ReperfusionInduced Arrhythmia: Comparison of Rats Fed Fish Oil With Controls Fed Omega-6 PUFA Oils

Sensitivity Analysis - Sequential Dropping of One Study
Random Effects Model - Risk Ratio (D&L method)

Study Dropped	Study Year	Size	Total N	Risk Ratio	95% CI Low	95% CI High	2P
Hock	1987	27	142	0.41	0.19	0.86	0.018
Hock	1990	43	126	0.64	0.19	2.14	0.47
McLennan	1993	22	147	0.47	0.23	0.96	0.038
McLennan	1993	27	142	0.48	0.24	0.97	0.041
Abeywardena	1995	36	133	0.48	0.23	0.97	0.040
McLennan	1990	14	155	0.46	0.23	0.92	0.028

Table 3-6. Total VF Deaths: Comparison of Monkeys Fed Tuna Fish Oil With Controls Fed Sunflower Seed Oil (Omega-6 PUFA) *

Author, Year	Omega-3 Arms	Dosage, g/100 g	Duration	Omega-3 Fatty Acids Event	Omega-3 Fatty Acids Total	Control Event	Control Total	Experiment Protocols
McLennan, 1992	Tuna	2.8	30 months	0	16	3	13	Control condition, ischemia, and isoproterenol (0.5 ug/kg body weight/minute) models

* Total ventricular fibrillation (VF) deaths were combined in control condition, ischemia, and isoproterenol models.

Table 3-7. Ventricular Tachycardia in Ischemia-Induced Arrhythmias: Comparison of Rats Fed Omega-3 Fatty Acids With Controls Fed Omega-6 PUFA Oils

Author, Year	Omega-3 Arms	Dosage, g/100 g	Duration	Omega-3 Fatty Acids		Control		RR (95% CI)	Experiment Protocols
				Event	Total	Event	Total		
ALA Oils									
Abeywardena, 1995	Soybean	0.4	9 months	8	18	7	18	1.1 (0.53-2.5)	5-min ischemia
McLennan, 1995	Soybean	1.1	12 weeks	8	13	13	14	0.66 (0.42-1.0)	15-min ischemia
McLennan, 1995	Canola	1.2	12 weeks	12	16	13	14	0.81 (0.591.1)	15-min ischemia
Isensee, 1994	Linseed	5.2	10 weeks	6	10	4	9	1.4 (0.56-3.3)	20-min ischemia
	Meta-analysis:	**Total subjects = 112**		**34**	**57**	**37**	**55**	**0.82 (0.65-1.0)**	**Random-effect model**
Fish Oils (EPA+DHA)									
Charnock, 1991	Fish oil	2.1	12 months	7	10	10	10	0. 71 (0.41-1.1)	15-min ischemia
McLennan, 1993	Fish oil	2.6	12 weeks	5	14	12	13	0.39 (0.19-0.79)	15-min ischemia
Isensee, 1994	Fish oil	3.0	10 weeks	0	10	4	9	0.10 (0.01-1.7)	20-min ischemia
Abeywardena, 1995	MaxEPA	3.3	9 months	1	18	7	18	0.14 (0.02-1.1)	5-min ischemia
McLennan, 1988	Tuna	3.7	12 months	2	10	8	10	0.25 (0.07-0.90)	15-min ischemia
McLennan, 1990	Tuna	3.7	18 months	4	7	4	7	1.0 (0.40-2.5)	15-min ischemia
	Meta-analysis:	**Total subjects = 136**		**19**	**69**	**45**	**67**	**0.49 (0.29-0.83)**	**Random-effect model**

Figure 3-3. Ventricular tachycardia in ischemia-induced arrhythmias: comparison of rats fed alpha linolenic acid (ALA) with controls fed omega-6 PUFA oils

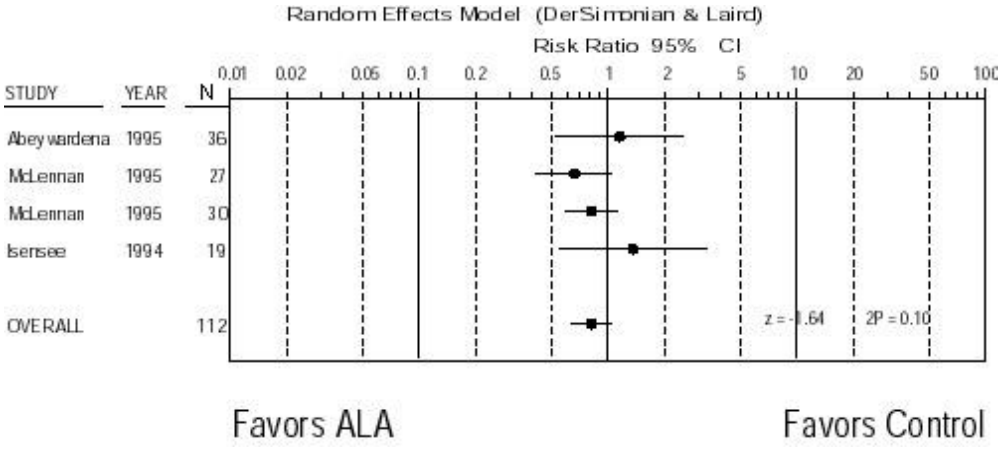

Figure 3-4. Ventricular tachycardia in ischemia-induced arrhythmias: comparison of rats fed fish oils with controls fed omega-6 PUFA oils

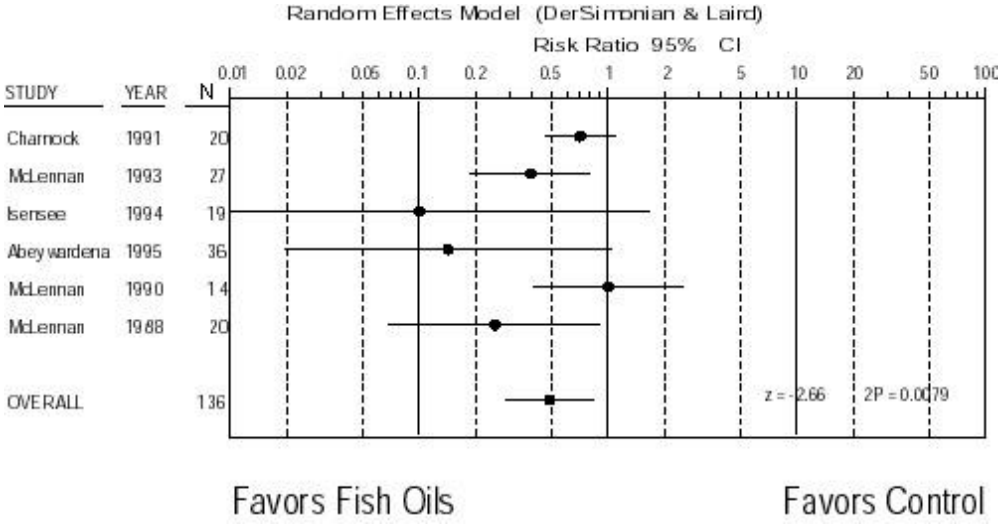

Table 3-8. Ventricular Tachycardia in Reperfusion-Induced Arrhythmias: Comparison of Rats Fed Omega-3 Fatty Acids With Controls Fed Omega-6 PUFA Oils

Author, year	Omega-3 Arms	Dosage, g/100 g	Duration	Omega-3 Fatty Acids		Control		RR (95% CI)	Experiment Protocols
				Event	Total	Event	Total		
ALA oils									
Abeywardena, 1995	Soybean	0.4	9 months	13	17	7	18	2.0 (1.0-3.7)	5-min Ischemia; 10-min Reperfusion
McLennan, 1995	Soybean	1.1	12 weeks	9	10	7	10	1.3 (0.82-2.0)	5-min Ischemia; 10-min Reperfusion
McLennan, 1995	Soybean	1.1	12 weeks	7	11	9	13	0.92 (0.52-1.6)	15-min Ischemia; 10-min Reperfusion
McLennan, 1995	Canola	1.2	12 weeks	7	10	7	10	1.0 (0.56-1.8)	5-min Ischemia; 10-min Reperfusion
McLennan, 1995	Canola	1.2	12 weeks	4	13	9	13	0.44 (0.18-1.1)	15-min Ischemia; 10-min Reperfusion
	Meta-analysis:	**Total subjects = 125**		**40**	**61**	**39**	**64**	**1.1 (0.73-1.6)**	**Random-effect model**
Fish Oils (EPA+DHA)									
Anderson, 1996	MaxEPA	41% of TT FAs	8 weeks	3 *	8	3 *	6	0.75 (0.23-2.5)	20-min ischemia; reperfusion
McLennan, 1993	Fish oil	2.6	12 weeks	6	10	10	12	0.72 (0.41-1.3)	5-min Ischemia; 5-min Reperfusion
McLennan, 1993	Fish oil	2.6	12 weeks	3	14	8	12	0.32 (0.11-1.0)	15-min ischemia; 5-min reperfusion
Abeywardena, 1995	MaxEPA	3.3	9 months	4	18	7	18	0.57 (0.20-1.6)	5-min ischemia; 10-min reperfusion
McLennan, 1988	Tuna	3.7	12 months	5	10	8	10	0.63 (0.31-1.3)	15-min ischemia; reperfusion
McLennan, 1990	Tuna	3.7	18 months	5	7	6	7	0.83 (0.48-1.5)	15-min ischemia; 10-min reperfusion
	Meta-analysis:	**Total subjects = 132**		**26**	**67**	**42**	**65**	**0.68 (0.50-0.91)**	**Random-effect model**

TT FAs = total fatty acids; RR = risk ratio; VF = ventricular fibrillation; VT = ventricular tachycardia

* Sustained VT and/or VF were excluded from the analyses

Figure 3-5. Ventricular tachycardia in reperfusion-induced arrhythmias: comparison of rats fed alpha linolenic acid (ALA) with controls fed omega-6 PUFA oils

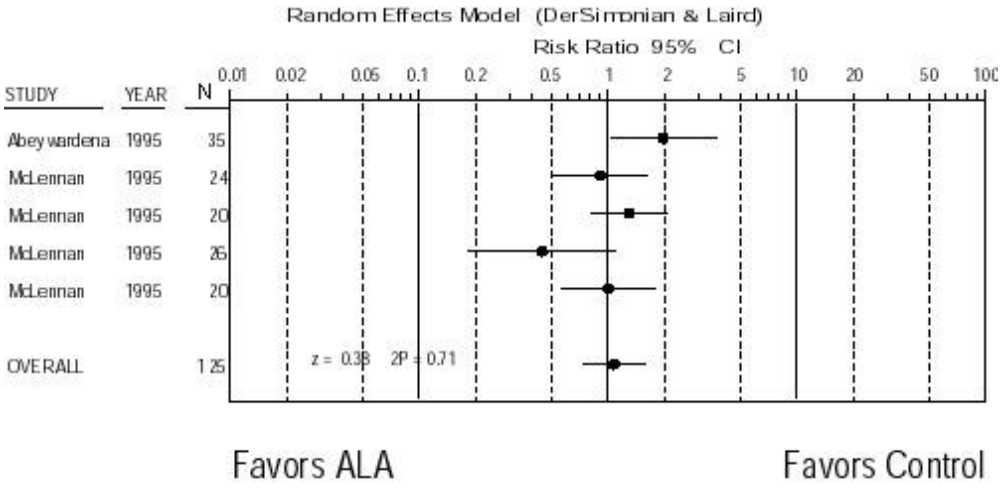

Figure 3-6. Ventricular tachycardia in reperfusion-induced arrhythmias: comparison of rats fed fish oils with controls fed omega-6 PUFA oils

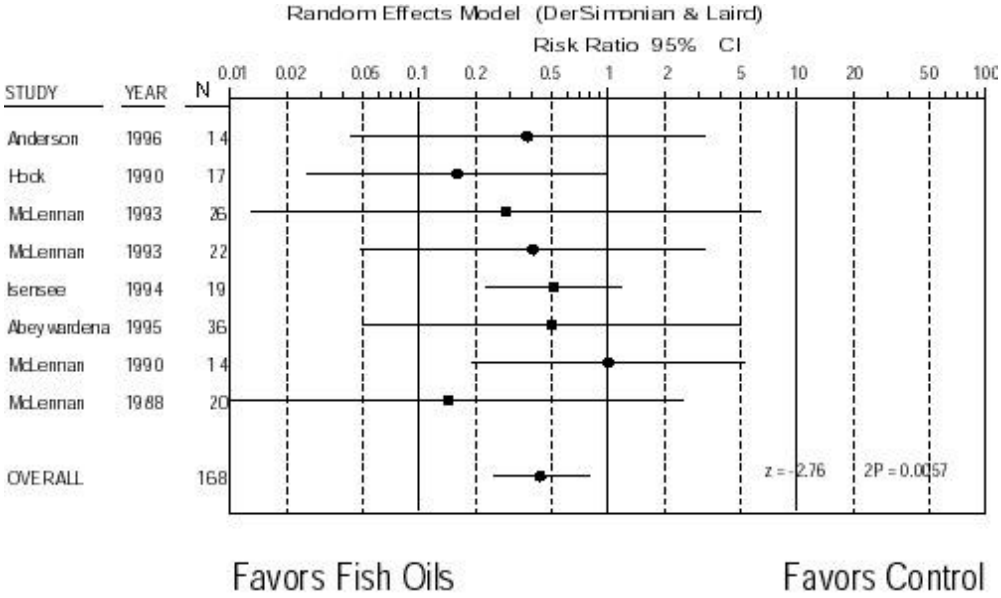

Table 3-9. Ventricular Fibrillation in Ischemia-Induced Arrhythmias: Comparison of Rats Fed Omega-3 Fatty Acids With Controls Fed Omega-6 PUFA Oils

Author, Year	Omega-3 Arms	Dosage, g/100 g	Duration	Omega-3 Fatty Acids		Control		RR (95% CI)	Experiment Protocols
				Event	Total	Event	Total		
ALA oils									
McLennan, 1995	Soybean	1.1	12 weeks	5	13	6	14	0.90 (0.36-2.2)	15-min ischemia
McLennan, 1995	Canola	1.2	12 weeks	7	16	6	14	1.0 (0.45-2.3)	15-min ischemia
Isensee, 1994	Linseed	5.2	10 weeks	4	10	4	9	0.90 (0.31-2.6)	20-min ischemia
	Meta-analysis: Total subjects = 76			**16**	**39**	**16**	**37**	**0.95 (0.56-1.6)**	**Random-effect model**
Fish Oils (EPA+DHA)									
Charnock, 1991	Fish oil	2.1	12 months	0	10	6	10	0. 08 (0.00-1.2)	15-min ischemia
McLennan, 1993	Fish oil	2.6	12 weeks	0	14	5	13	0.08 (0.01-1.4)	15-min ischemia
Isensee, 1994	Fish oil	3.0	10 weeks	1	10	4	9	0.22 (0.03-1.7)	20-min ischemia
McLennan, 1988	Tuna	3.7	12 months	0	10	1*	10	0.33 (0.02-7.3)	15-min ischemia
McLennan, 1990	Tuna	3.7	18 months	1	7	2	7	0.50 (0.06-4.3)	15-min ischemia
	Meta-analysis: Total subjects = 100			**2**	**51**	**18**	**49**	**0.21 (0.07-0.63)**	**Random-effect model**

* Estimated from graph

Figure 3-7. Ventricular fibrillation in ischemia-induced arrhythmias: comparison of rats fed alpha linolenic acid (ALA) with controls fed omega-6 PUFA oils

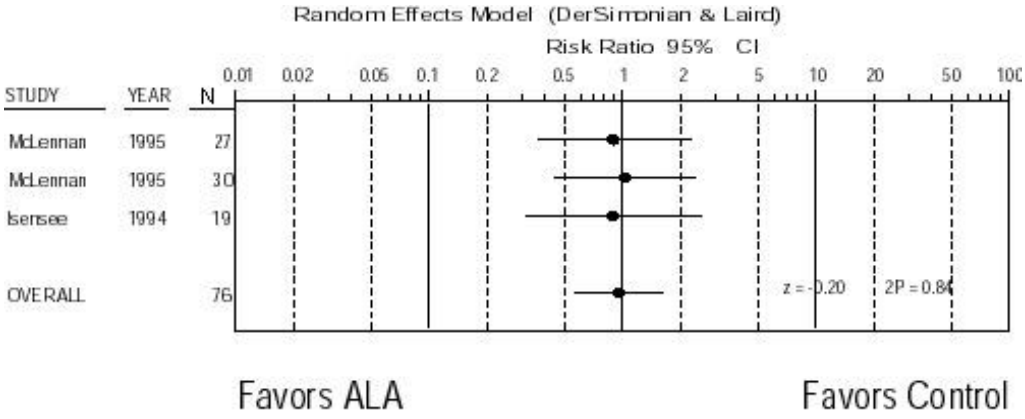

Figure 3-8. Ventricular fibrillation in ischemia-induced arrhythmias: comparison of rats fed fish oils with controls fed omega-6 PUFA oils

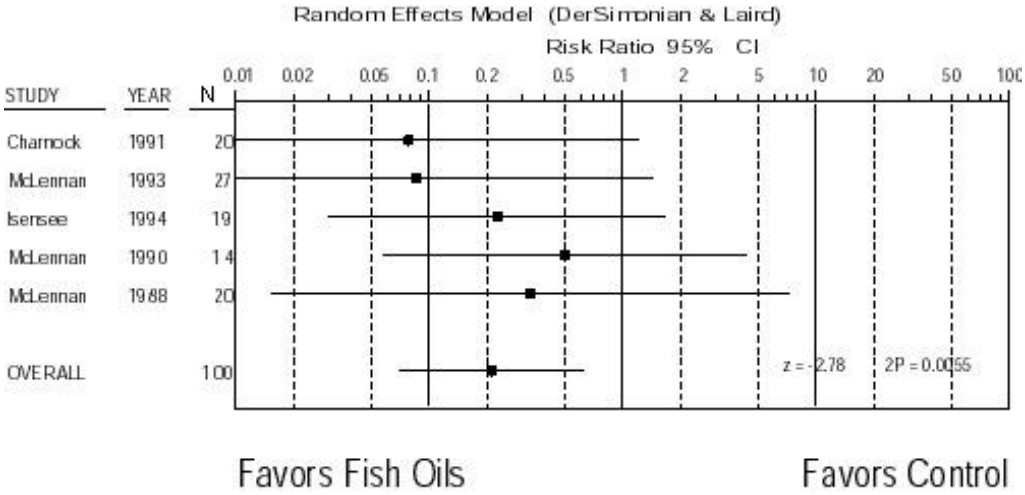

Table 3-10. Ventricular Fibrillation in Reperfusion-Induced Arrhythmias: Comparison of Rats Fed Omega-3 Fatty Acids With Controls Fed Omega-6 PUFA Oils

Author, Year	Omega-3 Arms	Dosage, g/100 g	Duration	Omega-3 Fatty Acids		Control		RR (95% CI)	Experiment Protocols
				Event	Total	Event	Total		
ALA Oils									
Abeywardena, 1995	Soybean	0.4	9 months	4	17	2	18	2.1 (0.44-10)	5-min ischemia; 10-min reperfusion
McLennan, 1995	Soybean	1.1	12 weeks	5	10	5	10	1.0 (0.42-2.4)	5-min Ischemia; Reperfusion
McLennan, 1995	Soybean	1.1	12 weeks	3	11	3	13	1.2 (0.30-4.7)	15-min ischemia; reperfusion
McLennan, 1995	Canola	1.2	12 weeks	1	10	5	10	0.20 (0.03-1.4)	5-min ischemia; reperfusion
McLennan, 1995	Canola	1.2	12 weeks	0	13	3	13	0.14 (0.01-2.5)	15-min ischemia; reperfusion
Isensee, 1994	Linseed	5.2	10 weeks	6	10	7	9	0.77 (0.42-1.4)	20-min ischemia; 20-min reperfusion
	Meta-analysis:	**Total subjects = 144**		**19**	**71**	**25**	**73**	**0.84 (0.52-1.3)**	**Random-effect model**
Fish Oils (EPA+DHA)									
Anderson, 1996	MaxEPA™	41% of TT FAs	8 weeks	1 *	8	2 *	6	0.38 (0.04-3.2)	20-min ischemia; reperfusion
Hock, 1990	Menhaden	1.2	4 weeks	1 †	7	9 †	10	0.16 (0.03-0.99)	15-min ischemia; 6-hr reperfusion
McLennan, 1993	Fish oil	2.6	12 weeks	1	10	3	12	0.40 (0.05-3.3)	5-min ischemia; 5-min reperfusion
McLennan, 1993	Fish oil	2.6	12 weeks	0	14	1	12	0.29 (0.01-6.5)	15-min ischemia; 5-min reperfusion
Isensee, 1994	Fish oil	3.0	10 weeks	4	10	7	9	0.51 (0.22-1.2)	20-min ischemia; 20-min reperfusion
Abeywardena, 1995	MaxEPA™	3.3	9 months	1	18	2	18	0.50 (0.05-5.0)	5-min ischemia; 10-min reperfusion
McLennan, 1988	Tuna	3.7	12 months	0	10	3	10	0.14 (0.01-2.5)	15-min ischemia; reperfusion
McLennan, 1990	Tuna	3.7	18 months	2	7	2	7	1.0 (0.19-5.2)	15-min ischemia; reperfusion
	Meta-analysis:	**Total subjects = 168**		**10**	**84**	**29**	**84**	**0.44 (0.25-0.79)**	**Random-effect model**

TT FA = total fatty acids; VT = ventricular tachycardia; VF = ventricular fibrillation
* Sustained VT and/or VF were excluded from the analyses
† VT or VF (%)

Figure 3-9. Ventricular fibrillation in reperfusion-induced arrhythmias: comparison of rats fed alpha linolenic acid (ALA) with controls fed omega-6 PUFA oils

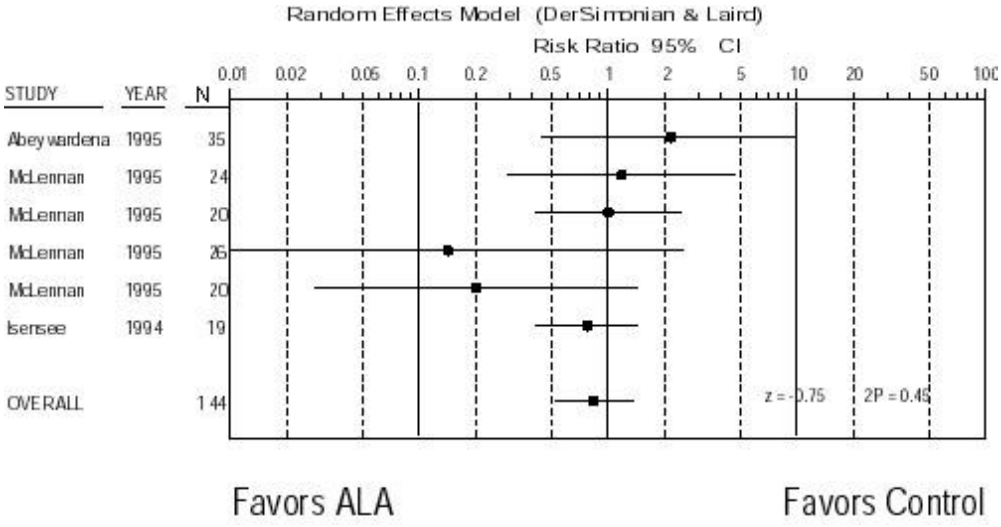

Figure 3-10. Ventricular fibrillation in reperfusion-induced arrhythmias: comparison of rats fed fish oils with controls fed omega-6 PUFA oils

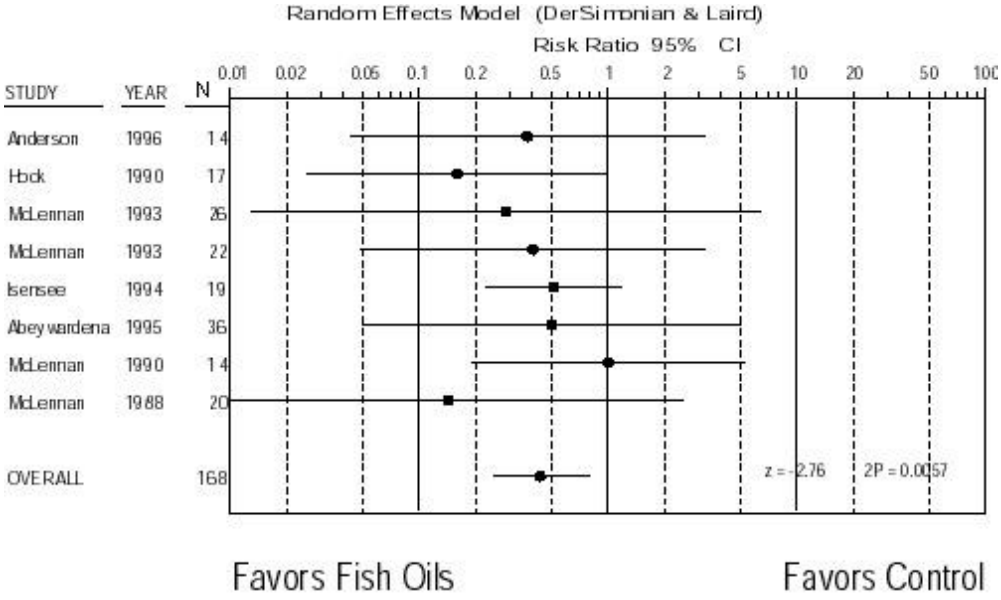

Table 3-11. Ventricular Fibrillation in Induced Arrhythmia: Comparison of Monkeys Fed Fish Oils With Controls Fed Sunflower Seed Oil (Omega-6 PUFA)

Author, Year	Omega-3 Arms	Dosage, g/100 g	Duration	Omega-3 Fatty Acids		Control		VFT ¶	Experiment Protocols
				Event	Total	Event	Total		
Electrical-Stimulation Arrhythmias †									
McLennan, Bridle, 1993	Fish oil	1.8	16 weeks	6	10	5	9	+133% *	Electrical stimulation in control condition
Charnock, 1992	Fish oil	2.4	16 weeks	8%	ND	13%	ND	NS	Electrical stimulation in control condition
McLennan, 1992	Tuna	2.8	30 months	10	16	8	13	NS	Electrical stimulation in control condition
Electrical-Stimulation Arrhythmias in Ischemic Hearts †									
McLennan, Bridle, 1993	Fish oil	1.8	16 weeks	10	10	9	9	+79% *	Electrical stimulation + 5-min ischemia
Charnock, 1992	Fish oil	2.4	16 weeks	Nil	ND	13%	ND	NS	Electrical stimulation + ischemia
McLennan, 1992	Tuna	2.8	30 months	12	16	8	13	NS	Electrical stimulation + 5-min ischemia
Electrical-Stimulation Arrhythmias With Isoproterenol †									
McLennan, Bridle, 1993	Fish oil	1.8	16 weeks	3	10 ‡	7	9 ‡	+55% *	Electrical stimulation + 30-min isoproterenol (0.5 ug/kg BW/min)
McLennan, Bridle, 1993	Fish oil	1.8	16 weeks	5	10 ‡	9	9 ‡	+75%	Electrical stimulation + 30-min isoproterenol (2.0 ug/kg BW/min)
McLennan, 1992	Tuna	2.8	30 months	7	16	10	13	NS	Electrical stimulation + 30-min Iisoproterenol (0.5 ug/kg BW/min)

ND = no data; BW = body weight; min = minute; VFT = ventricular fibrillation threshold, measured only in VF inducible animals; NS = no significant difference compared to controls

* $P<0.05$ compared to control animals

† Same monkeys underwent electrical stimulation in control condition, 5 minutes after ischemia. procedure, and 30 minutes after restoration of coronary blood flow during the infusion of isoproterenol.

‡ Same monkeys injected 0.5 ug/kg BW/min isoproterenol, then the dosage of isoproterenol was increased to 2.0 ug/kg BW/min.

¶ An increase in VFT is a desirable outcome for antiarrhythimic effects. See Chapter 2: Methods for the effects expressed as percent change.

Table 3-12. Ventricular Premature Beats/Complex, Infarct Size, Arrhythmia Score and Length of Time in Normal Sinus Rhythm: Comparison of Rats Fed Omega-3 Fatty Acids With Controls Fed Omega-6 PUFA Oils

Author, Year	Omega-3 Arms	Dosage, g/100 g	Duration	Total N	Arrhythmia Outcomes [1]				Experimental Protocols
					VPB	AS [2]	IS	TSR [3]	
ALA Oils									
Abeywardena, 1995	Soybean	0.4	9 months	36	+176%	+107%*	-	-	5-min ischemia; 10-min reperfusion
McLennan, 1995	Canola	1.1	5 weeks	30	-13%	-11%	-	-	15-min ischemia
					-43%	-64%	-	-	10-min reperfusion
McLennan, 1995	Canola	1.1	5 weeks	20	-19%	–41%*	-	-	5-min ischemia; 10-min reperfusion
Isensee, 1994	Linseed	5.2	10 weeks	20	-	-	NS	NS	20-min ischemia
McLennan, 1995	Soybean	1.2	5 weeks	27	-14%	-18%	-	-	15-min ischemia
					-2%	-12%	-	-	10-min reperfusion
McLennan, 1995	Soybean	1.2	5 weeks	20	+34%	+30%	-	-	5-min ischemia; 10-min reperfusion
Fish Oils (EPA+DHA)									
Anderson, 1996	MaxEPA	41% of TT FAs	8 weeks	14	-31%	-54%	-	-	20-min ischemia; reperfusion
Hock, 1990	Menhaden	1.0	4 weeks	17	-	-77% †	-	-	15-min ischemia; 6-hr reperfusion
Hock, 1987	Menhaden	1.0	4 weeks	23	NC	-	-	-	15-min after ischemia w/o reperfusion
Charnock, 1991	Fish oil	2.1	12 months	20	-72%*	-59%*	-	-	15-min ischemia
McLennan, 1993	Fish oil	2.6	12 weeks	27	-10% -31%	-41%* -63%*	- -	+12% +2%	15-min ischemia 5-min reperfusion
McLennan, 1993	Fish oil	2.6	12 weeks	22	-27%	-48%	-	+16%	5-min ischemia; 5-min reperfusion
Isensee, 1994	Fish oil	3.0	10 weeks	20	-	-	NS	Increased*	20-min ischemia
Abeywardena, 1995	MaxEPA	3.3	9 months	36	-13%	-40%	-	-	5-min ischemia; 10-min reperfusion
McLennan, 1990	Tuna	3.7	18 months	14	+6% -24%*	NS NS	-	-5% +21%	15-min ischemia 10-min reperfusion
McLennan, 1988	Tuna	3.7	12 months	20	-	NS -44%*	+7%, NS	-	15-min ischemia reperfusion

TT FAs = total fatty acids; VPB = ventricular premature beats/complex; IS = infarct size/size of ischemia zone; AS = arrhythmia score (according to Curtis et. al.); TSR =length of time in normal sinus rhythm; ISO = Isoproterenol
- Not reported NS = no significant difference compared to controls
* $P<0.05$ compared to controls † $P<0.01$ compared to controls

[1] See Methods for the effects expressed as percent change.
[2] AS in all studies were calculated according to Curtis et al [Cardiovascular Research 22, 656-665], except Hock, 1990 used a modified method
[3] An increase in TSR is a desirable outcomes for antiarrhythmic effects.

Table 3-13. Arrhythmic Effects in Studies Comparing Omega-3 Long-Chain PUFAs with a Linolenic Acid

Author, Year	Omega-3 Arms	Dosage, g/100 g	Duration	Animal	Sample Size	Arrhythmia Outcomes							Experimental Protocols
						Deaths	VT	VF	VPB /10 min	IS	AS	TSR ¶, min	
Abeywardena, 1995	Soybean	0.4	9 months	Rats	18	11%	76%	23%	298	-	3.1	-	5-min ischemia
	MaxEPA	3.3	9 months	Rats	18	0%	22%	5%	94	-	0.9	-	10-min reperfusion
Isensee, 1994	Linseed	5.2	10 weeks	Rats	10	-	60% -	40% 60%	-	35%* -	-	5.5*† -	20-min ischemia 20-min reperfusion
	Fish oil	3.0	10 weeks	Rats	10	-	0% -	10% 40%	-	36%* -	-	10*† -	20-min ischemia 20-min reperfusion

VT = ventricular tachycardia; VF = ventricular fibrillation; VPB = ventricular premature beats; IS = infarct size/size of ischemia zone;
AS = arrhythmia score (according to Curtis et. al.); TSR = length of time in normal sinus rhythm; min = minute
- Not reported * estimated value from figures † $p<0.05$ between groups
¶ An increase in TSR is a desirable outcomes for antiarrhythmic effects

Table 3-14. Total Deaths in Ischemia-Reperfusion-Induced Arrhythmias: Comparison of Animals Fed Fish Oil (EPA+DHA) With Controls Fed Saturated Fats

Author, year	Omega-3 Arms	Dosage, g/100 g	Duration	Omega-3 Fatty Acids		Control		Experiment Protocols
				Event	Total	Event	Total	
Rabbits								
Chen, 1994	Fish oil	5.2 %kcal	2 weeks	3 *	12	5 *	14	10-min ischemia; 1-hr reperfusion
Chen, 1994	Fish oil	5.2 %kcal	2 weeks	6 †	14	8 †	15	1-hr ischemia; 4-hr reperfusion
Piglets								
Hartog, 1987	Mackerel	0.6	16 weeks	1	7	0	6	5-min ischemia; 10-min reperfusion

* Two deaths in each group occurred during reperfusion
† 50% deaths occurred during ischemia; 50% occurred during reperfusion

Table 3-15. Ventricular Tachycardia in Ischemia-Reperfusion-Induced Arrhythmias: Comparison of Animals Fed Fish Oil With Controls Fed Saturated Fats

Author, Year	Omega-3 Arms	Dosage, g/100 g	Duration	Omega-3 Fatty Acids		Control		Experiment Protocols
				Event	Total	Event	Total	
Rats								
Pepe, 1996	Fish oil	5.2	16 weeks	7 †	20	14 †	20	15-min ischemia; 10-min reperfusion
Piglets								
Hartog, 1987	Mackerel	0.6	16 weeks	2 *	7	1 *	6	5-min ischemia; 10-min reperfusion

[1] All events occurred during ischemia procedure
† Some events occurred during ischemia; some occurred during reperfusion

Table 3-16. Ventricular Fibrillation in Ischemia-Reperfusion-Induced Arrhythmias: Comparison of Animals Fed Fish Oil With Controls Fed Saturated Fats

Author, Year	Omega-3 Arms	Dosage, g/100 g	Duration	Omega-3 Fatty Acids		Control		Experiment Protocols
				Event	Total	Event	Total	
Rats								
Pepe, 1996	Fish oil	5.2 %kcal	16 weeks	0	20	16	20	15-min ischemia; 10-min reperfusion
Yang, 1993	Fish oil	5.4 %kcal	5 days	3 *	8	7 *	9	15-min ischemia; 10-min reperfusion
Piglets								
Hartog, 1987	Mackerel	0.6	16 weeks	3 †	7	0	6	5-min ischemia; 10-min reperfusion

* VT (%) or VF (%). All events occurred during reperfusion
† Some events occurred during ischemia; some occurred during reperfusion

Table 3-17. Ventricular Premature Beats in Ischemia-Reperfusion-Induced Arrhythmias: Comparison of Animals Fed Fish Oil With Controls Fed Saturated Fats

Author, Year	Omega-3 Arms	Dosage, g/100 g	Duration	Animals	Total N	VPB [1]	Experiment Protocols
Ischemia-Induced Arrhythimas							
Chen, 1994 [2]	Fish oil	5.2 %kcal	2 weeks	Rabbits	22	-50% -35%	10-min ischemia 1-hr ischemia
Hartog, 1987	Mackerel	0.6	16 weeks	Piglets	13	+53%	5-min ischemia
Pepe, 1996	Fish oil	5.2 %kcal	5 days	Rats	40	-73%*	15-min ischemia
Reperfusion-Induced Arrhythimas							
Chen, 1994 [2]	Fish oil	5.2 %kcal	2 weeks	Rabbits	22	0% -25%	10-min ischemia; 1-hr reperfusion 1-hr ischemia; 4-hr reperfusion
Hartog, 1987	Mackerel	0.6	16 weeks	Piglets	13	-65%*	15-min ischemia; 10-min reperfusion

VPB = ventricular premature beat
*P<0.05

[1] See Chapter 2: Methods for the effects expressed as percent change
[2] Study results were biased by excluding more subjects who died from arrhythmias in the control group

Table 3-18. Total Deaths in Induced Arrhythmias: Comparison of Dogs Fed EPA and/or DHA With No Treatment Controls

Author, Year	Omega-3 Arms	Dosage, g/100 g	Duration	Omega-3 Fatty Acids		Control		Experiment Protocols
				Event	Total	Event	Total	
Culp, 1980	Menhaden	3.3 %kcal	5~7 weeks	3	10	5	17	Coronary artery thrombosis induced by electrical stimulation
Otsuji, 1993	EPA ester	1.0	8 weeks	0	10	5	15	Coronary artery ligation (or ischemia)

Table 3-19. Ventricular Premature Beats/Complex, Infarct Size, Arrhythmia Score and Areas at Risk of Arrhythmias: Comparison of Dogs Fed EPA and/or DHA With No Treatment Controls

Author, Year	Omega-3 Arms	Dosage, g/100 g	Duration	Total N	Arrhythima Outcomes [1]				Experimental Protocols
					VPB	AS [3]	IS	ARAr	
Kinoshita, 1994	EPA ester	1.0	8 weeks	20	-44%*	-55% †	-	-	3-hr ischemia
Culp, 1980	Menhaden	3.3 %kcal	5~7 weeks	27	Decreased	-	-52%	-	Electrical stimulation
Otsuji, 1993 [2]	EPA ester	1.0	8 weeks	20	-	-	-40% †	NS	Ischemia
Oskarsson, 1993	MaxEPA	1.0	6 weeks	22	-	-	-55%*	NS	90-min ischemia; 30-min reperfusion

VPB = ventricular premature beats/complex; IS = infarct size/size of ischemia zone; AS = arrhythima score (according to Curtis et al, 1987); TSR =length of time in normal sinus rhythm; ARAr = areas at risk of arrhythmias; ISH = ischemia
- Not reported NS = no significant difference compared to controls
* *P*<0.05 compared to controls † p<0.01 compared to controls

[1] See Chapter 2: Methods for the effects expressed as percent change
[2] Study results were biased by excluding more subjects who died from arrhythmias in the control group

Table 3-20. Effects of Intravenously Infused Omega-3 Fatty Acids on Ischemia-Induced or Spontaneous Arrhythmias in Mongrel Dogs

Author, Year	Omega-3 Arms (N)	Dosage	Controls (N)	Results	Experiment Protocols
Billman, 1994	10 ml fish oil conc (n=4), or 5 ml fish oil + 5 ml Tg conc (n=4)	Fish oil conc.: 70% EPA+DHA T conc.: 65% EPA+DHA	Saline (n=3) or lipid emulsion (n=5)	N / VF incidence Fish oil infusion 8 13%* Controls 8 100% *P<0.005 compared to controls	Exercise-ischemia (2-min) test
Billman, 1999	Albumin-bound ALA (n=8) EPA (n=7) DHA (n=8)	98% EPA 91% DHA >99% ALA No data on the amount (ml) infused	SBO lipid emulsion, containing 7%~8% ALA (n=7)	N / VF incidence ALA 8 25%* EPA 7 29%* DHA 8 25%* Controls 7 100% *P<0.05 compared to controls	Exercise-ischemia (2-min) test
Lo, 1991	ALA (n=8) [1]	1, 5, 10, 20, 30, or 60 mg/kg	Control buffer, pH 8.1 (no lipids)	Eight dogs were infused control buffer or different doses of ALA. No events of VT or VPB were observed when infusing control buffer, or ALA up to 10 mg/kg. ALA (mg/kg): 20, 30, 60 VPC: 25%, 75%*, 88%* VT: 13%, 38%, 63%* *P<0.05 compared to control buffer	Normal condition

Tg = triglyceride; VF = ventricular fibrillation; VPC = ventricular premature complex; VT = ventricular tachycardia; conc = concentrate; SBO = soybean oil

[1] A left atrial injection instead of intravenous injection was used as the route of administration in this study

Table 3-21. Effects of Omega-3 Fatty Acids on Contractile Parameters in Whole Animal Isolated Organ and Cell Studies

Author, Year	Animal Model [Type, Age, Sex]	Exposure Duration (Weeks)	Comparison Groups[a]		Amount of Omega-3 Fatty Acid	Experimental Condition	Agent[b]	Heart Rate	Contractility[c]	IP[d]	Cardiac Work
			Omega-3 Fatty Acid (n)	Control (n)							
RAT											
Chemla, 1995	Myocardium, Adult, Male	4	N-3 (15)	N-3 (16)	15%wt	Ambient	None		NC (FVR)		
Demaison, 1993	Isolated heart, weanling, male	8	LIN (29)	SF (32)	100g/kg	Ambient	None				NC
Heard, 1992	Atrial tissue, adult, male	4	FO+SAF (6-11)	SAF (6-11)	19.5%+0.5%wt	Ambient	ISO		NC (FOC)		
			FO+SAF (6-11)	SAF (6-11)	19.5%+0.5%wt	Ambient	Saline	NC	NC (FOC) NC (df/dt) NC (–df/dt)		
			FO+SAF (6-11)	SAF (6-11)	19.5%+0.5%wt	Ambient	LPS	D*	I* (FOC) I* (df/dt) I* (–df/dt)		
Ku, 1997	Isolated heart, aged female	12	HC+EPA	HC	300mg/kg	Ambient	None	NC			
			HC+DHA	HC	300mg/kg	Ambient	None	NC			
			HC+DHA	HC+EPA	300mg/kg	Ambient	None	NC			
Leifert, 2000	Ventricular myocyte, young adult, male (Gavage)	3	FO (29-36)	LARD (29-36)	35g/d	Ambient	None			NC (DCL) NC (SCL) NC (PCL) NC (PRP)	
			FO (6 animals)	LARD (6 animals)	35g/d	Ambient	ISO		D*		
			FO (6-9 animals)	LARD (6-9 animals)	35g/d	Ambient	FRGS		D*		
Leifert, 2001	Ventricular myocyte, adult male	3	FO (6 animals)	SF (6 animals)	10%wt	Ambient	ISO		D*** D* (Time) NC (#)		
Reig, 1993	Ventricular tissue, young adult, male	5	FO (5)	HF (5)	6%wt	Ambient	None	NC			

Table 3-21. Effects of Omega-3 Fatty Acids on Contractile Parameters in Whole Animal Isolated Organ and Cell Studies

Author, Year	Animal Model [Type, Age, Sex]	Exposure Duration (Weeks)	Comparison Groups[a]		Amount of Omega-3 Fatty Acid	Experimental Condition	Agent[b]	Heart Rate	Contractility[c]	IP[d]	Cardiac Work
			Omega-3 Fatty Acid (n)	Control (n)							
Laustiola, 1986	Atrial myocyte, weanling, male	16	CLO (7-11)	Std (7-11)	10% wt	High O_2	None	D***		D*** (A)	
			CLO (4-11)	Std (4-11)	10% wt	High O_2	NA	NC		NC (A)	
			CLO (4-11)	Std (4-11)	10% wt	Hypoxia	NA	D***		D*** (A)	
			CLO (4-11)	Std (4-11)	10% wt	Reoxygenation	NA	NC		NC (A)	

IP= inotropic parameters; D = decrease; I = increase; NA = not applicable ; NC = no change; ND= no data; * = p<0.05 ** = p<0.01; *** = p<0.001

A = amplitude
CLO = cod liver oil
D = decrease
DCL =diastolic cell length
df/dt =maximum rate of rise of contraction
DHA =decosahexaenoic acid
EPAe =EPA esters
FO = fish oil
FOC =force of contraction
FRGS =free radical generating system
FVR =force-velocity relationship
HC = high cholesterol
HF = high fat
ISO =isoproteronol
LIN = linseed oil
LPS =lipopolysaccharide
PCL =percent cell length
PRP =post rest potentiation
SAF = safflower oil
SF = saturated fat
STD = standard chow

Table 3-22. Effects of Omega-3 Fatty Acids on Basoelectromechanical Parameters in Whole Animal Isolated Organ and Cell Studies

Author, Year	Animal Model [Type, Age, Sex]	Exposure Duration (Weeks)	Comparisons[a]		Amount of Omega-3	Experiment Condition	Agent	VERP	ARP	RRP	QRS	QT	MAP	RDT
			Omega-3 Fatty Acid (n)	Control (n)										
RAT														
Reig, 1993	Ventricular, young adult, male	5	FO+HF (5)	HF (5)	6+31% wt	Ambient	None	D*						
Karmazyn, 1987	Isolated heart weanling male/female	12	CLO (5-9)	STD (5-9)	10% wt	Ischemia Reperfusion	None							NC
RABBIT														
Gillis, 1992	SR vesicles, weanling, ND	6	FO (9)	SAF (9)	10% wt	Ambient	None	NC	NC	NC	NC	NC	NC epi NC endo	

VERP =left ventricular effective refractory period; ARP = absolute refractory period ; RRP =relative refractory period ;
QRS =ventricular conductance time; Qt = electrocardiogram interval ; MAP =monophasic action potential duration ; RDT = developed or resting tension;
D = decrease; I = increase; NA = not applicable ; NC = no change; ND= no data; * = $p<0.05$ ** = $p<0.01$; *** = $p<0.001$

CLO = cod liver oil
D = decrease
endo =endocardial
epi =epicardial
FO = fish oil
HF = high fat
NC =no change
ND =no data
SAF = safflower oil
STD =standard chow
SR =sarcoplasmic reticulum

Table 3-23. Effects of Omega-3 Fatty Acids on Ion Pumps and Ion Movement in Whole Animal Isolated Organ and Cell Studies

Author, Year	Animal Model [Type, Age, Sex]	Feeding Duration (Weeks)	Comparison Groups[a]		Am-mount of Omega-3	Experiment Condition	Agent	Pump[a] Activity	Cys Ca^{2+} Influx	Cys Ca^{2+} Efflux	Cys Ca^{2+} Content	SR Ca^{2+} Content	SR Ca^{2+} Release	SR Ca^{2+} Uptake
			Omega-3 Fatty Acid (N)	Control (N)										
MOUSE														
Croset, 1989b	SR vesicles, weanling, male	2	ALA ester (3)	SAF (3)	0.5%wt	Ambient	None					D*		
			EPA ester (3)	SAF (3)	0.5%wt	Ambient	None	NC SR $_{Ca2+Mg2+}$				D*		
			DHA ester (3)	SAF (3)	0.5%wt	Ambient	None	NC SR $_{Ca2+Mg2+}$				D*		
Swanson, 1989	SR vesicles, weanling, male	2	SAF+FO (3ht)	SAF+CO (3ht)	10% wt	Ambient	None	D* Ca2+Mg2+						D**
Croset, 1989a	SR vesicles, weanling, male	2	DHA ester (10)	STD (10)	0.4 g/100 g	Ambient	None	NC SR $_{Ca2+Mg2+}$						
			DHA ester (10)	STD (10)	0.8 g/100 g	Ambient	None	NC SR $_{Ca2+Mg2+}$						
			DHA ester (10)	STD (10)	4 g/100 g	Ambient	None	NC SR $_{Ca2+Mg2+}$						
	Cardiac, weanling, male	2	DHA ester (10)	STD (10)	0.4 g/100 g	Ambient	Oligomycin	I* $_{Ca2+Mg2+}$						
			DHA ester (10)	STD (10)	0.8 g/100 g	Ambient	Oligomycin	I* $_{Ca2+Mg2+}$						
			DHA ester (10)	STD (10)	4 g/100 g	Ambient	Oligomycin	NC $_{Ca2+Mg2+}$						
RAT														
Benedikts-dottir, 1988	Cardiac, adult male	16	Cod liver (ND)	Corn (ND)	!0% wt	Ambient	None	NC $_{Na+K+}$						
Pepe, 1999	Cardiac, aged & young adults, male	2	Fish oil (5)	Omega-6 (6)	11.7% wt	Ambient	None				NC			
			Fish oil (5)	Omega-6 (6)	11.7% wt	Ambient w/ NorEpi	None				D* total D* aged NC young			
			Fish oil (5)	Omega-6 (6)	11.7% wt	15-minute ischemia; 5-minute reperfusion	None				D* aged D*** young			

Table 3-23. Effects of Omega-3 Fatty Acids on Ion Pumps and Ion Movement in Whole Animal Isolated Organ and Cell Studies

Author, Year	Animal Model [Type, Age, Sex]	Feeding Duration (Weeks)	Comparison Groups[a]		Am-mount of Omega-3	Experiment Condition	Agent	Pump[a] Activity	Cys Ca^{2+} Influx	Cys Ca^{2+} Efflux	Cys Ca^{2+} Content	SR Ca^{2+} Content	SR Ca^{2+} Release	SR Ca^{2+} Uptake
			Omega-3 Fatty Acid (N)	Control (N)										
Taffet, 1993	SR vesicle, young adult, female	3	CO+FO (11-12)	CO (11-12)	17% wt	Ambient	None							D*
			CO+FO (11-12)	CO (11-12)	17% wt	Ambient	Ca2+ 50uM ATP	D* SR Ca2+Mg2+ D* Ca2+						
			CO+FO (11-12)	CO (11-12)	17% wt	Ambient	Ca2+ 50uM ATP+ Ionomycin	D* SR Ca2+Mg2+ D* Ca2+ NC Mg2+						
			CO+FO (11-12)	CO (11-12)	17% wt	Ambient	Ca2+ 1 mM ATP+ Ionomycin	D* Ca2+Mg2+ D* Ca2+ D*Mg2+				D*		
Leifert, 2001	Cardiac, adult, male	3	Fish oil (8)	SFA (8)	10% wt	Ambient					NC	NC		
			Fish oil (8)	SFA (8)	10% wt	Ambient	Caffeine					NC		
			Fish oil (8)	SFA (8)	10% wt	Ambient	DBHQ					NC		I* Ca2+ exchanger efflux
			Fish oil (8)	SFA (8)	10% wt	Ambient	ISO				NC			I* Ca2+ exchanger or SR efflux
Black, 1989	SR, adult, male (Gavage)	4	FO (6)	STD(6)	0.5 ml/kg/d	Ambient	Ca^{2+}							NC Ca2+ transport activity
Karmazyn, 1987	Ventricular, weanling, male/female	12	Cod liver (5-9)	STD (up to 11)	10%wt	20-minute ischemia; 30-minute reperfusion	None		I**	NC				
Maixent, 1999	Cardiac, adult, male	8	Fish oil (4)	STD (4)	0.5 g/kg	Ambient	OUA	NC Na+K+						

Table 3-23. Effects of Omega-3 Fatty Acids on Ion Pumps and Ion Movement in Whole Animal Isolated Organ and Cell Studies

Author, Year	Animal Model [Type, Age, Sex]	Feeding Duration (Weeks)	Comparison Groups[a]		Am-mount of Omega-3	Experiment Condition	Agent	Pump[a] Activity	Cys Ca^{2+} Influx	Cys Ca^{2+} Efflux	Cys Ca^{2+} Content	SR Ca^{2+} Content	SR Ca^{2+} Release	SR Ca^{2+} Uptake
			Omega-3 Fatty Acid (N)	Control (N)										
Chen, 1994	Cardiac, adult, male	2	Fish oil (5)	Coconut (5)	10%wt	Ischemia	None				NC			
			Fish oil (5)	Coconut (5)	10%wt	10-minute ischemia; 1-hour reperfution	None				NC			
			Fish oil (5)	Coconut (5)	10%wt	1-hour ischemia; 4-hour reperfusion	None				NC			
Kinoshita, 1994	Cardiac, adult ND	8	EPA ester (6)	STD (ND)	100 mg/kg/d	Ambient	None	I* $_{Ca2+Mg2+ (Vmax)}$ NC $_{Km}$						
			EPA ester (6)	STD (ND)	100 mg/kg/d	Ischemic	None	I* $_{Ca2+Mg2+ (Vmax)}$ NC $_{Km}$						
			EPA ester (6)	STD (ND)	100 mg/kg/d	Ambient	OUA	NC $_{Na+K+}$						
			EPA ester (6)	STD (ND)	100 mg/kg/d	Ischemic	OUA	NC $_{Na+K+}$						
Honen, 2002	Atrial, adult, male	3	Fish oil (6)	Canola (6)	3 ml/d	Ambient	None		NC					
PIG														
Lamers, 1988	Sarcolemma, weanling, male/female	8	Fish oil (8)	Lard (8)	4.5%w	Ambient	Ca^{2+}	I*$_{Ca2+}$						
						Ischemia Reper-fusion	Ca^{2+}	I*$_{Ca2+}$						

Cys= cytosolic; SR= sarcoplasmic reticulum; D = decrease; I = increase; NC = no change; ND= no data; * = p<0.05 ** = p<0.01; *** = p<0.001

ALAe =alpha linoleic acid
ATP =adenosine triphosphate
CO = corn oil
D = decrease
DBHQ =2,4-Di-tert-buytlhydroquinone
DHA =decosahexaenoic acid
EPAe =eicosapentaenoic acid
FO = fish oil
I =increase
ISO =isoproteronol
Mg2+=magnesium
NC =no change
ND =no data
OUA =ouabain
SAF = safflower oil
SFA =saturated fatty acid
STD =standard chow
SR =sarcoplasmic reticulum
uM =micromoles

Table 3-24. Effects of Omega-3 Fatty Acids on Ion Currents In Whole Animal Isolated Organ and Cell Studies

Author, year	Animal Model [Type, Age, Sex]	Exposure Duration (weeks)	Comparison Group[a]		Amount of Omega-3	Expt. Condition	Agent	I_{Na}	I_{to}	I_{CaL}	I_K	I_{KI}	I_{KUR}
			Omega-3 Fatty Acid (n)	Control (n)									
RAT													
Minarovic, 1998	ventricular myocyte, Young adult, male	2	FO (ND)	HF (ND))	100g/Kg/d	Ambient	None			NC Ac NC InAc NC A			
Leifert, 2000	ventricular myocyte, Young adult, male	3	FO (17-28)	LARD (17-28)	29% Energy	Ambient	None	NC Ac NC InAc	NC Ac NC InAc				

I_{Na}=initial fast current; I_{to}= transient K+ outward current or initial outward current; $I_{Ca.L}$= voltage dependent L-type Calcium current/inward current/calcium sparks; I k= delayed rectifier K+ current; I_{ki}= inward rectifier K+ current; I_{kur}= ultra rapid K+ current; Ac-activation parameter; InAc = inactivation parameter; D = decrease; I = increase; NC = no change; ND= no data; * = p<0.05 ** = p<0.01; *** = p<0.001

A =amplitude
Ac =activation parameter
FO = fish oil
InAc =inactivation parameter
HF = high fat
NC =no change

Table 3-25. Effects of Omega-3 Fatty Acids on Ion Channels In Whole Animal Isolated Organ and Cell Studies

Author, year	Animal Model [Type, Age, Sex]	Exposure Duration (weeks)	Comparison Groups[a]		Amount of omega-3	Experimental Condition	Agent[b]	Binding to the Ca^{2+} Channel
			Omega-3 FA (n)	Con-trol (n)				
RAT								
Gudmunds -dottir, 1991	Ventricular SL, Adult, male	20	CLO (4-5)	CO (4-5)	10% wt	Ambient	NIT	NC K_d NC B_{max}
	Ventricular SL, Aged, male	88	CLO (4-5)	CO (4-5)	10% wt	Ambient	NIT	NC K_d NC B_{max}
	Ventricular SL, Adult & aged, male	20 & 88	CLO (5)	CO (5)	10% wt	Ambient	NIT	D* K_d NC B_{max}
Minarovic, 1997	Ventricular myocytes, Young adult, male	2	FO (ND)	HF (ND)	100g/kg	Ambient	VER	No effect of agent
			FO (ND)	HF (ND)	100g/kg	Ambient	DIL	No effect of agent

D = decrease; I = increase; NC = no change; ND= no data; * = $p<0.05$ ** = $p<0.01$; *** = $p<0.001$

CLO = cod liver oil
CO = corn oil
D = decrease
DIL =diltiazem
FA =fatty acid
FO = fish oil
HF = high fat
NC =no change
ND =no data
NIT =nitrendipine
VER =verapamil

Table 3-26. Effects of Omega-3 Fatty Acids on Arrhythmogenic and Contractile Parameters in Isolated Organ and Cell Culture Studies

Author, Year	Model [Animal, Age, Type]	Exposure Duration	Comparison Groups[a]		Amount of Omega-3	Experimental Condition	Agent[b]	AR[c]	Con-Tractility[d]	IP	tC_{20}	CD_{20}	CD_{80}	$-C_{max}$	$+C_{max}$
			Omega-3 Fatty Acid (n)	Control (n)											
RAT															
Hallaq, 1992	Rat, neonatal, ventricular	1-2 min Free	DHA (6)	STD (6)	5uM	Ambient	None		NC						
			DHA (10)	STD (10)	5uM	Ambient	OUA	P* T*							
			DHA (6)	STD (6)	5uM	Ambient	NIT		B*						
			DHA (4)	STD (4)	5uM	Ambient	BAY		B*						
			DHA (3-4)	STD (3-4)	5uM	Ambient	VER		NB						
			DHA (3-4)	STD (3-4)	5uM	Ambient	DIL		NB						
			EPA (ND)	STD (ND)	5uM	Ambient	OUA	P*							
Jahangiri, 2000	Rat, adult, atrial	7 minFree	EPA (107/7ht)	STD (107/7ht)	10uM	Ambient	ISO		D**						
			DHA (101/5ht)	STD (101/5ht)	10uM	Ambient	ISO		D*						
			DHA m.e. (71/4ht)	STD (71/4ht)	10uM	Ambient	ISO		NC						
Kang & Leaf, 1994	Rat, neonatal, cardiac	3 minFree	ALA (5)	STD (5)	5-10uM	Ambient	None		D*						
			EPA (46)	STD (46)	5-10uM	Ambient	None		D*	NC A					
			EPA (ND)	STD (ND)	5-10uM	Ambient	Var[a]		D*						
			EPA (ND)	STD (ND)	5-10uM	Ambient	Ca^{2+}	P* T*							
			EPA (ND)	STD (ND)	5-10uM	Ambient	OUA	P* T*							
			EPAe.e. (3)	STD (3)	5-10uM	Ambient	None		NC						
			DHA (32)	STD (32)	5-10uM	Ambient	None		D*	NC A					
			DHA (ND)	STD (ND)	5-10uM	Ambient	Ca^{2+}	P* T*							
			DHA (ND)	STD (ND)	5-10uM	Ambient	OUA	P* T*							

Table 3-26. Effects of Omega-3 Fatty Acids on Arrhythmogenic and Contractile Parameters in Isolated Organ and Cell Culture Studies

Author, Year	Model [Animal, Age, Type]	Exposure Duration	Comparison Groups[a]		Amount of Omega-3	Experimental Condition	Agent[b]	AR[c]	Con-Tractility[d]	IP	tC_{20}	CD_{20}	CD_{80}	$-C_{max}$	$+C_{max}$
			Omega-3 Fatty Acid (n)	Control (n)											
Kang & Leaf, 1996	Rat, neonatal, cardiac	3-7 min Free	ALA (5)	STD (5)	10-15uM	Ambient	LPC	P*	D*						
		3-7 min Free	ALA (5)	STD (5)	10-15uM	Ambient	PTC	P* T*							
		3-7 min Free	EPA (5)	STD (5)	10-15uM	Ambient	LPC	P* T*	D*						
		3-7 min Free	EPA (5)	STD (5)	10-15uM	Ambient	PTC	P* T*							
		3-7 min Free	EPA (5)	STD (5)	10-15uM	Ambient	Ca^{2+} Ionophore	P* T*							
		3-7 min Free	EPA (7)	STD (7)	15uM	Ambient	Electrical pacing		D** EA						
		3-7 min Free	DHA (5)	STD (5)	10-15uM	Ambien	LPC	P*	D*						
		3-7 min Free	DHA (5)	STD (5)	10-15uM	Ambient	PTC	P* T*							
Kang, 1995b	Rat, neonatal, cardiac	5 min Free	EPA (4)	STD (4)	8uM	Ambient	Cholera toxin		D^{ND}						
			EPA (5-8)	STD (5-8)	5-10uM	Ambient	ISO	P* T*	D^{ND}						
			EPA (3)	STD (3)	5-10uM	Ambient	ISO+INDO+ BW	P*							
			EPA (5)	STD (5)	5-10uM	Ambient	cAMP	T*							
			DHA (3)	STD (8)	5-10uM	Ambient	ISO+INDO+ BW	P*							
Leifert, 2000	Rat, adult, ventricular	ND Free	DHA (5)	DA (5)	10uM	Ambient	ISO		D**						
			DHA (4)	Stearic A (4)	10uM	Ambient	LPC		D**						
			DHA (4)	Stearic A (4)	10uM	Ambient	ISO		D*						

Table 3-26. Effects of Omega-3 Fatty Acids on Arrhythmogenic and Contractile Parameters in Isolated Organ and Cell Culture Studies

Author, Year	Model [Animal, Age, Type]	Exposure Duration	Comparison Groups[a]		Amount of Omega-3	Experimental Condition	Agent[b]	AR[c]	Contractility[d]	IP	tC_{20}	CD_{20}	CD_{80}	$-C_{max}$	$+C_{max}$
			Omega-3 Fatty Acid (n)	Control (n)											
Li, 1997	Rat, neonatal, cardiac	ND Free	EPA (ND)	STD (ND)	10uM	Ambient	Eico	T*	D*						
MacLeod, 1998	Rat,adult, ventricular	5 min Free	EPA (6-8)	STD (6-8)	1-7.5uM	Ambient	None		I[ND] TS						
			EPA (6-8)	STD (6-8)	>10uM	Ambient	None		D[ND] TS						
			DHA (6-8)	STD (6-8)	1-7.5uM	Ambient	None		I[ND] TS						
			DHA (6-8)	STD (6-8)	>10uM	Ambient	None		D[ND] TS						
Negretti, 2000	Rat, adult ventricular	ND Free	EPA (6-57)	STD (6-57)	10uM	Ambient	None		D*** F	I*** RCL					
Pepe, 1994	Rat, adult, cardiac	4 min Free	DHA (6)	STD (6)	5 uM	Ambient	None		NC DL NC TA NC VS/DL						
			DHA (6)	STD (6)	5 uM	Ambient	NIT		B* TA B* VS/DL						
			DHA (6)	STD (6)	5 uM	Ambient	ISO		NC TA NC DL						
			DHA (6)	STD (6)	5 uM	Ambient	BAY		B* TA B* VS/DL						
Rodrigo, 1999	Rat, adult, ventricular	10 min Free	EPA (8)	STD (8)	5uM	Ambient	None		D***TS						
	Rat, adult, SSP ventricular	10 min Free	EPA (5)	STD (5)	5uM	Ambient	Ca^{2+}		D* F NC Relax						
			EPA (5)	STD (5)	10uM	Ambient	Ca^{2+}		D* F NC Relax						
Weylandt, 1996	Rat, neonatal, cardiac	3-12min Free	EPA (8)	STD (8)	15uM	Ambient	ISO	T*							
			EPA (12)	STD (12)	15uM	Ambient	Ca^{2+}	D*							
			DHA (8)	STD (8)	15uM	Ambient	ISO	T*							
			DHA (12)	STD (12)	15uM	Ambient	Ca^{2+}	D*							
		3-12 min Free 48 hr Bound	DHA Free (23)	DHA Bound (23)	15uM	Ambient	ISO	T*							
			EPA Free (23)	EPA Bound (23)	15uM	Ambient	ISO	T*							

Table 3-26. Effects of Omega-3 Fatty Acids on Arrhythmogenic and Contractile Parameters in Isolated Organ and Cell Culture Studies

Author, Year	Model [Animal, Age, Type]	Exposure Duration	Comparison Groups[a]		Amount of Omega-3	Experimental Condition	Agent[b]	AR[c]	Contractility[d]	IP	tC_{20}	CD_{20}	CD_{80}	$-C_{max}$	$+C_{max}$
			Omega-3 Fatty Acid (n)	Control (n)											
			DHA Free (10)	DHA Bound (10)	15uM	Ambient	Ca^{2+}	D*							
			EPA Free (10)	EPA Bound (10)	15uM	Ambient	Ca^{2+}	D*							
Courtois, 1992	Rat, neonatal, ventricular	24 hr Bound	SM3-Na-Al (5)	STD (5)	28%ALA+ 30%EPA	Ambient	None		NC				NC	NC	NC
			SM3-Na-Al (5)	STD (5)	28%ALA+ 30%EPA	Ambient	ISO		D*				NC	NC	NC
			SM3-Na-Al (5)	SM6-Na-Al (5)	28%ALA+ 30%EPA	Ambient	None		NC				NC	NC	I**
			SM3-Na-Al (5)	SM6-Na-Al (5)	28%ALA+ 30%EPA	Ambient	ISO		NC				NC	NC	NC
De Jonge, 1996	Rat, neonatal, ventricular	4-5 d Bound	EPA (4)	STD (4)	214uM	Ambient	None		D*						
Durot, 1997	Rat, neonatal, ventricular	4 d Bound	SM3 (6)	SM6 (6)	25uM EPA+ 25 uM DHA-Al	Ambient	None				NC	NC	NC	NC	NC
			SM3 (6)	SM6 (6)	25uM EPA+ 25uM DHA-Al	Hypoxia	None				NC	NC	NC	NC	NC
			SM3 (6)	SM6 (6)	25uM EPA+ 25uM DHA-Al	Reoxy	None				NC	NC	NC	NC	NC
Fournier, 1995	Rat, neonatal, ventricular	4 d Bound	EPA (11)	DHA (11)	100uM	Ambient	None				NC	NC	NC	NC	NC
Grynberg, 1988	Rat, neonatal, ventricular	24 h Bound	SM3 (11)	SM6 (11)	57%ALA +7%LA +0.2% AA-Na-Al	Ambient	None				NC		NC		
			SM3 (11)	SM6 (11)	57%ALA +7%LA +0.2% AA-Na-Al	Hypoxia	None				NC		NC		

Table 3-26. Effects of Omega-3 Fatty Acids on Arrhythmogenic and Contractile Parameters in Isolated Organ and Cell Culture Studies

Author, Year	Model [Animal, Age, Type]	Exposure Duration	Comparison Groups[a]		Amount of Omega-3	Experimental Condition	Agent[b]	AR[c]	Contractility[d]	IP	tC_{20}	CD_{20}	CD_{80}	$-C_{max}$	$+C_{max}$
			Omega-3 Fatty Acid (n)	Control (n)											
			SM3 (11)	SM6 (11)	57%ALA +7%LA +0.2% AA-Na-Al	Reoxy	None				NC		NC		
Grynberg, 1995	Rat, neonatal, ventricular	4 d Bound	EPA-Na-Al (12)	DHA-Na-Al (12)	100uM	Ambient	None		NC F			NC	NC	NC	NC
			EPA-Na-Al (6)	DHA-Na-Al (6)	100uM	Ambient	ISO		D* F				NC		
			EPA-Na-Al (6)	DHA-Na-Al (6)	100uM	Ambient	Phe		NC				NC		
			EPA-Na-Al (6)	DHA-Na-Al (6)	100uM	Ambient	dBcAMP		D*						
Grynberg, 199	Rat, neonatal, ventricular	4 d Bound	EPA-Al (10)	DHA-Al (10)	0.1mM	Ambient	None		NC			NC	NC	NC	NC
		4 d Bound	EPA-Al (10)	DHA-Al (10)	0.1mM	Ambient	Phe		NC						
		4 d Bound	EPA-Al (10)	DHA-Al (10)	0.1mM	Ambient	ISO		D**						
		4 d Bound	EPA-Al (10)	DHA-Al (10)	0.1mM	Ambient	dBcAMP		D**						
Hallaq, 1990	Rat, neonatal	3-5 d Bound	EPA (6)	STD (6)	5uM	Ambient	None		NC	NC A					
			EPA (6)	STD (6)	5uM	Ambient	OUA		D***	I*** A					
Ponsard, 1999	Rat, neonatal, ventricular	4 d Bound	EPA+DHA-Al (13)	STD (13)	5%EPA+ 7%DHA	Ambient	None		NC			NC	NC	NC	NC
			EPA+DHA-Al (7)	N-6 (7)	5%EPA+ 7%DHA	Ambient	ISO		I*			NC	NC	NC	NC
			EPA+DHA-Al (6)	N-6 (6)	5%EPA+ 7%DHA	Ambient	PHE		I*			NC	NC	NC	NC

Table 3-26. Effects of Omega-3 Fatty Acids on Arrhythmogenic and Contractile Parameters in Isolated Organ and Cell Culture Studies

Author, Year	Model [Animal, Age, Type]	Exposure Duration	Comparison Groups[a]		Amount of Omega-3	Experimental Condition	Agent[b]	AR[c]	Contractility[d]	IP	tC_{20}	CD_{20}	CD_{80}	$-C_{max}$	$+C_{max}$
			Omega-3 Fatty Acid (n)	Control (n)											
Reithman, 1996	Rat, neonatal, cardiac	3 d Bound	DHA (15)	STD (15)	60uM	Ambient	NA+TIM	D**							
Weylandt, 1996	Rat, neonatal, cardiac	48 hr Bound	EPA (107)	STD (51)	15uM	Ambient	ISO	NC							
			EPA (20)	STD (14)	15uM	Ambient	Ca^{2+}	NC							
			DHA (51)	STD (13)	15uM	Ambient	ISO	NC							
			DHA (20)	STD (6)	15uM	Ambient	Ca^{2+}	NC							
			EPA (107)	DHA (51)	15uM	Ambient	ISO	NC							
			EPA (6-14)	DHA (6-14)	15uM	Ambient	Ca^{2+}	NC							
GUINEA PIG															
Ferrier, 2002	Guinea pig, adult, ventricular	15-20 min Free	DHA m.e. (18-24)	STD (18-24)	10uM	Ambient	None		D***CICR NC VSRM						
Juan, 1987	Guinea pig, adult, isolated heart	30 min Free	EPA-Na (8)	STD (8)	$6x10^{-8}$ mol/min	Ambient	OvAl	NC							
			EPA-Na (8)	STD (8)	$15x10^{-8}$ mol/min	Ambient	OvAl	D*							
			EPA-Na (5)	STD (5)	$15x10^{-8}$ mol/min	Ambient	OvAl+Es	D*							
MacLeod, 1998	Guinea pig, adult, ventricular	5 min Free	EPA (6-8)	STD (6-8)	5-20uM	Ambient	None		D^{ND} TS dd						
			DHA (6-8)	STD (6-8)	5-20uM	Ambient	None		D^{ND} TS dd						
Rodrigo, 1999	Guinea pig, adult, ventricular	10 min Free	EPA (7)	STD (7)	5uM	Ambient	None		D***TS						
	Guinea pig, adult, SSP ventricular	10 min Free	EPA (5)	STD (5)	5uM	Ambient	Ca^{2+}		D* F NC Relax						

Table 3-26. Effects of Omega-3 Fatty Acids on Arrhythmogenic and Contractile Parameters in Isolated Organ and Cell Culture Studies

AR= arrhthymia; IP= inotropic parameters; tC_{20}= contracting coupling delay; CD_{20}= contraction delay at 20% relaxation ; CD_{80}= contraction delay at 80% relaxation ; $-C_{max}$= relaxation time; $+C_{max}$= cell shortening velocity; D = decrease; I = increase; NC = no change; ND= no data; * = $p<0.05$ ** = $p<0.01$; *** = $p<0.001$

A =amplitude	DHA m.e. =decosahexaenoic acid methylated	LPC =lysophosphatidylcholine	RCL =resting cell length
AI =adequate intake	DIL =diltiazem	N-6 =omega-6	SM3 =synthesized medium for omega-3 group
ALA =alpha linoleic acid	DL =diastolic length	NA+TIM =sodium and timolol	SM6 = synthesized medium for omega-6 group
AR =arrhythmia	Eico =eicosanoids	NB =no block	STD = standard chow
B =blocked	EPA =eicosapentaenoic acid	NC =no change	T =terminated
BAY =Bay K8644	EPAe.e. = eicosapentaenoic acid ethylated	ND =no data	TA =twitch amplitude
BW = BW 755c lipoxygenase inhibitor	Es =esculetin	NIT =nitrendipine	TS =twitch size
cAMP =cyclic adenosine monophosphate	F =frequency	OUA =ouabain	uM=micromoles
CICR =calcium induced contractile response	INDO =indomethacin	OvAI =ovalbumin	VER =verapamil
D = decrease	IP =inotropic parameters	P =prevented	VS/DL=velocity of shortening/diastolic length
DA =amplitude	ISO =isoproteronol	PHE =phenylephrine	VSRM =voltage sensitive release mechanism
dBcAMP =dibutyryl cyclic adenosine monophosphate	LA =linoleic acid	PTC =palmitoylcamitine	

Table 3-27. Effects of Omega-3 Fatty Acids on Basoelectromechanical Parameters in Isolated Organ and Cell Culture Studies

Author, Year	Model [Animal, Type, Age]	Exposure Duration	Omega-3 Fatty Acid (n)	Con-trol (n)	Amount of Omega-3	Experi-mental Condition	Agent	AP	APA	APD_{40}	APD_{80}	V_{max}	MDP	OS	Other
RAT															
Bogdanov, 1998	Rat, adult ventricular	10-15 min Free	EPA (ND)	STD (ND)	5-10uM	Ambient	None	I[ND]	NC						
			EPA (ND)	STD (ND)	20uM	Ambient	None		D[ND]	I[ND]		D[ND]			
			DHA (ND)	STD (ND)	10-50uM	Ambient	None		D[ND]	I[ND]		D[ND]			
Kang, 1995	Rat, neonatal, ventricular	2-5 min Free	EPA (8)	STD (8)	10uM	Ambient	None	D* F D**	NC		D**	NC			
MacLeod, 1998	Rat, adult, ventricular	5 min Free	EPA (11-14)	STD (11-14)	1-7.5uM	Ambient	None				I[ND] dd				
			EPA (11-14)	STD (11-14)	>10uM	Ambient	None				D[ND] dd				
			DHA (6-8)	STD (6-8)	1-7.5uM	Ambient	None				I[ND]				
			DHA (11-14)	STD (11-14)	>10uM	Ambient	None				D[ND] dd				
Durot, 1997	Rat, neonatal, ventricular	4 d Bound	SM3 (9)	SM6 (9)	25uM EPA+ 25uM DHA-Al	Ambient	None	NC	NC	NC	NC	I*	NC	NC	
			SM3 (5)	SM6 (5)	25uM EPA+ 25uM DHA-Al	Hypoxia	None	NC	D*	D**	D*	NC	NC		
			SM3 (5)	SM6 (5)	25uM EPA+ 25uM DHA-Al	Reoxy	None	NC	NC	NC	NC	NC	Im		
Fournier, 1995	Rat, neonatal, ventricular	4 d Bound	EPA (11)	DHA (11)	100uM	Ambient	None	NC	I*	NC	NC	NC	NC	I*	
Grynberg, 1988	Rat, neonatal, ventricular	24 h Bound	SM3 (11)	SM6 (11)	57%ALA+ 7% LA+ +0.2% AA-Na-Al	Ambient	None	NC	NC	NC	NC	NC	NC	NC	
			SM3 (11)	SM6 (11)	57%ALA+ 7% LA+ +0.2% AA-Na-Al	Hypoxia	None	NC	D**	NC	NC	NC	NC	D*	

Table 3-27. Effects of Omega-3 Fatty Acids on Basoelectromechanical Parameters in Isolated Organ and Cell Culture Studies

Author, Year	Model [Animal, Type, Age]	Exposure Duration	Omega-3 Fatty Acid (n)	Con-trol (n)	Amount of Omega-3	Experi-mental Condition	Agent	AP	APA	APD_{40}	APD_{80}	V_{max}	MDP	OS	Other
			SM3 (11)	SM6 (11)	57%ALA+ 7% LA +0.2% AA-Na-Al	Reoxy	None	NC	I**	NC	NC	NC	NC	I*	
Grynberg, 1996	Rat, neonatal, ventricular	4 d Bound	EPA-Al (10)	DHA-Al (10)	0.1mM	Ambient	None		I*		NC	NC	NC	I*	
Reithman, 1996	Rat, neonatal, cardiac	3 d Bound	DHA (28-29)	STD (28-29)	60uM	Ambient	None	NC	I*						
			DHA (14-19)	STD (14-19)	60uM	Ambient	NA+TIM	D*							
			DHA (10-11)	STD (10-11)	60uM	Ambient	ISO	D*							
			DHA (4)	STD (4)	60uM	Ambient	OUA	D*							
GUINEA PIG															
MacLeod, 1998	Guinea pig, adult, ventricular	5 min Free	EPA (12-16)	STD (12-16)	1-20uM	Ambient	None				D^{ND} dd				
			DHA (12-16)	STD (12-16)	1-20uM	Ambient	None				D^{ND} dd				
CAT															
Bayer, 1979	Cat, adult, **heart** in situ	5 min Free IV	ALA-Na (7)	STD (7)	2mg/kg/ min	Ambient	INDO								NC_{AC} NC_{AVC} NC_{ARP} NC_{AVRP}

NC = no change; AP=action potential rate; APA= action potential amplitude; APD40= action potential duration at 40% depolarization; APD 80= action potential duration at 80% depolarization; Vmax= maximum rate of depolarization; MDP= maximum diastolic potential; OS= overshoot; D = decrease; I = increase; NC = no change; ND= no data; * = p<0.05 ** = p<0.01; *** = p<0.001

Table 3-27. Effects of Omega-3 Fatty Acids on Basoelectromechanical Parameters in Isolated Organ and Cell Culture Studies

AA =arachidonic acid	D = decrease	ISO= isoproteronol	OS= overshoot
AC =intra-atrial conduction time	dd =dose dependent	LA =linoleic acid	SM3 = synthesized medium for omega-3 group
ALA = alpha linoleic acid	DHA =decosahexaenoic acid	MDP= maximum diastolic potential	SM6 = synthesized medium for omega-6 group
ARP =functional refractory period of the atrium	F =frequency	N-6 =omega 6	STD = standard chow
AVC =atrioventricular conductance time	I =increased	ND =no data	SR =sarcoplasmic reticulum
AVRP =functional refractory period of atrioventricular conducting system	INDO =indomethacin		uM =micromoles

Table 3-28. Effects of Omega-3 Fatty Acids on Ion Pumps and Ion Movement in Isolated Organ and Cell Culture Studies

Author, Year	Model [Animal, Type, Age]	Exposure Duration	Comparison Groups		Amount of Omega-3	Experimental Condition	Agent	Pump Activity	Cys. Ca^{2+} influx	Cys. Ca^{2+} efflux	Cys Ca^{2+} Content	SR Ca^{2+} Content	SR Ca^{2+} Uptake	SR Ca^{2+} Release	Exchanger	Other
			Omega-3 Fatty Acid (n)	Control (n)												
RAT																
Kang & Leaf, 1996	Rat, neonatal, cardiac	7min Free	EPA (6)	STD (6)	10-15uM	Ambient	None				NCs_{ys} NC_{dia}					
			EPA (6)	STD (6)	10-15uM	Ambient	LPC				T_{CaFlu}					
Negretti, 2000	Rat, ND ventricular	ND Free	EPA (46)	STD (46)	10uM	Ambient	Ca^{2+}				D*** Bas					
			EPA (4)	STD (4)	5uM	Ambient	Caff					I*				
			DHA (3)	STD (3)	5uM	Ambient	Caff					I*				
O'Neill, 2002	Rat, ND ventricular	ND Free	EPA (6)	STD (6)	10uM	Ambient	Ca^{2+}		D*	NC	D^{ND} Bas					
			EPA (12)	STD (12)	10uM	Ambient	Caff			NC						
Pepe, 1994	Rat, young adult, cardiac	4 min Free	DHA (6)	STD (6)	5uM	Ambient	None				NC					
			DHA (6)	STD (6)	5uM	Ambient	NIT		B*		B*					
			DHA (6)	STD (6)	5uM	Ambient	BAY		B*		B*					
			DHA (6)	STD (6)	5uM	Ambient	ISO				NC					
Rinaldi, 2002	Rat, adult, ventricular	20 min vs 3 d Free	DHA+KCl (9)	DHA+KCL (9)	10uM	Ambient	KCl				*D* * mag of I					
			DHA (9)	DHA (9)	10uM	Ambient	KCl				*D* ** mag of I					
			DHA (9)	DHA (9)	10uM	Anoxia	None				D**					
			DHA (9)	DHA (9)	10uM	Anoxia	KCl				D**					
			DHA (9)	DHA (9)	10uM	Anoxia	ET-1				D**					

Table 3-28. Effects of Omega-3 Fatty Acids on Ion Pumps and Ion Movement in Isolated Organ and Cell Culture Studies

Author, Year	Model [Animal, Type, Age]	Exposure Duration	Comparison Groups		Amount of Omega-3	Experimental Condition	Agent	Pump Activity	Cys. Ca^{2+} influx	Cys. Ca^{2+} efflux	Cys Ca^{2+} Content	SR Ca^{2+} Content	SR Ca^{2+} Uptake	SR Ca^{2+} Release	Exchanger	Other
			Omega-3 Fatty Acid (n)	Control (n)												
		20 min free	DHA+ ET-1 (9)	STD (9)	10uM	Ambient	ET-1				I**					
			DHA (9)	STD (9)	10uM	Ambient	ET-1				*D* ** mag of I					
			DHA (9)	STD (9)	10uM	Ambient	None				NC_{bas}					
			DHA +KCl (9)	STD (9)	10uM	Ambient	KCl				I***					
			DHA (9)	STD (9)	10uM	Ambient	KCl				*D* ** mag of I					
			DHA+ET-1 (9)	STD (9)	10uM	Ambient	ET-1				*D* ** mag of I					
			DHA (9)	STD (9)	10uM	Ambient	ET-1				*D* ** mag of I					
			DHA (9)	STD (9)	10uM	Anoxia	None				*D* ** mag of I					
			DHA (9)	STD (9)	10uM	Anoxia	KCl				D**					
			DHA (9)	STD (9)	10uM	Anoxia	ET-1				D**					
		3 d Free	DHA (9)	STD (9)	10uM	Ambient	None				NC_{bas}					
			DHA+KCl (9)	STD (9)	10uM	Ambient	KCl				I***					
			DHA (9)	STD (9)	10uM	Ambient	KCl				*D* ** mag of I					
			DHA (9)	STD (9)	10uM	Anoxia	None				D**					
			DHA (9)	STD (9)	10uM	Anoxia	KCl				D**					
			DHA (9)	STD (9)	10uM	Anoxia	ET-1				D**					

Table 3-28. Effects of Omega-3 Fatty Acids on Ion Pumps and Ion Movement in Isolated Organ and Cell Culture Studies

Author, Year	Model [Animal, Type, Age]	Exposure Duration	Comparison Groups		Amount of Omega-3	Experimental Condition	Agent	Pump Activity	Cys. Ca^{2+} influx	Cys. Ca^{2+} efflux	Cys Ca^{2+} Content	SR Ca^{2+} Content	SR Ca^{2+} Uptake	SR Ca^{2+} Release	Exchanger	Other
			Omega-3 Fatty Acid (n)	Control (n)												
Rodrigo, 1999	Rat, adult, SSP ventricular	10 min Free	EPA (5)	STD (5)	5uM	Ambient	Ca^{2+}							D*		
			EPA (5)	STD (5)	10uM	Ambient	Ca^{2+}							D*		
Vitelli, 2002	Rat, adult, ventricular	20 min Free	DHA (ND)	STD (ND)	10uM	Ambient	Ca^{2+} free KRB				NC_{bas}					
			DHA (ND)	STD (ND)	10uM	Ambient	$CaCl_2$ KRB				NC_{bas}					
			DHA+ DXR (ND)	STD+ DXR (ND)	10uM	Ambient	DXR+ Ca^{2+} free KRB				D**			I*		
			DHA+ DXR (ND)	STD (ND)	10uM	Ambient	DXR+ Ca^{2+} free KRB				NC					
			DHA+ DXR (ND)	DHA (ND)	10uM	Ambient	DXR+ Ca^{2+} free KRB				NC					
			DHA+ DXR (9)	STD+ DXR (9)	10uM	Ambient	DXR+ CaCl2 KRB				D**			I*		
			DHA+ DXR (9)	STD (9)	10uM	Ambient	DXR+ CaCl2 KRB				NC					
			DHA+ DXR (9)	DHA (9)	10uM	Ambient	DXR+ CaCl2 KRB				NC					
			DHA (9)	STD (9)	10uM	Ambient	Caff+ $CaCl_2$ Free KRB				D**			I*		

Table 3-28. Effects of Omega-3 Fatty Acids on Ion Pumps and Ion Movement in Isolated Organ and Cell Culture Studies

Author, Year	Model [Animal, Type, Age]	Exposure Duration	Comparison Groups		Amount of Omega-3	Experimental Condition	Agent	Pump Activity	Cys. Ca^{2+} influx	Cys. Ca^{2+} efflux	Cys Ca^{2+} Content	SR Ca^{2+} Content	SR Ca^{2+} Uptake	SR Ca^{2+} Release	Exchanger	Other
			Omega-3 Fatty Acid (n)	Control (n)												
			DHA+ DXR (9)	STD (9)	10uM	Ambient	Caff+CaCl$_2$ Free KRB				NC					
			DHA (9)	STD (9)	10uM	Ambient	Caff+ CaCl2 KRB				D**			I*		
			DHA+ DXR (9)	STD (9)	10uM	Ambient	Caff+CaCl2 KRB				NC					
Xiao, 1997	Rat, adult ventricular	ND Free	EPA (ND)	STD (ND)	1.5uM	Ambient	None									D**$_{calcium\ transients}$
			EPA (ND)	STD (ND)	15uM	Ambient	None									D**$_{calcium\ transients}$
Hallaq, 1990	Rat, neonatal, cardiac	3-5d Bound	EPA (8)	STD (8)	5uM	Ambient	None				NC					
		3-5d Bound	EPA (3)	STD (3)	5uM	Ambient	OUA (1uM)				NC					
		3-5d Bound	EPA (5)	STD (5)	5uM	Ambient	OUA (0.1mM)				D***					
		3-5d Bound	EPA (10)	STD (10)	5uM	Ambient	OUA (0.1mM)	NC NaK								
		3-5d Bound	EPA (11)	STD (11)	5uM	Ambient	BUME	NC NaK								
		3-5d Bound	EPA (8)	STD (8)	5uM	Ambient	OUA+ BUME	NC NaK								
	Rat, neonatal, ventricular	4d Bound	DHA (4-11)	STD (4-11)	5uM	Ambient	OUA		B* I							
		4d Bound	DHA (5-14)	STD (5-14)	5uM	Ambient	NIT		BND D							
		4d Bound	DHA+NIT (5-14)	DHA (5-14)	5uM	Ambient	NIT		NC							
		4d Bound	DHA (5-14)	STD (5-14)	5uM	Ambient	BAY		BND I							

Table 3-28. Effects of Omega-3 Fatty Acids on Ion Pumps and Ion Movement in Isolated Organ and Cell Culture Studies

Author, Year	Model [Animal, Type, Age]	Exposure Duration	Comparison Groups		Amount of Omega-3	Experimental Condition	Agent	Pump Activity	Cys. Ca^{2+} influx	Cys. Ca^{2+} efflux	Cys Ca^{2+} Content	SR Ca^{2+} Content	SR Ca^{2+} Uptake	SR Ca^{2+} Release	Exchanger	Other
			Omega-3 Fatty Acid (n)	Control (n)												
		4d Bound	DHA+ BAY (5-14)	DHA (5-14)	5uM	Ambient	BAY		NC							
		4d Bound	DHA (5-14)	STD (5-14)	5uM	Ambient	OUA + NIT		B[ND] D							
		4d Bound	DHA +OUA + NIT (5-14)	DHA (5-14)	5uM	Ambient	OUA + NIT		NC							
		4d Bound	DHA+Bay +NIT (5-14)	STD+Bay +NIT	5uM	Ambient	BAY + NIT		B[ND] D							
		4d Bound	DHA+Bay +NIT (5-14)	DHA (5-14)	5uM	Ambient	BAY + NIT		NC							
		4d Bound	EPA (5-14)	STD (5-14)	5uM	Ambient	NIT		B[ND] D							
		4d Bound	EPA+NIT (5-14)	EPA (5-14)	5uM	Ambient	NIT		NC							
		4d Bound	EPA (5-14)	STD (5-14)	5uM	Ambient	BAY		B[ND] I							
		4d Bound	EPA+BAY (5-14)	EPA (5-14)	5uM	Ambient	BAY		NC							
		4d Bound	EPA (5-14)	STD (5-14)	5uM	Ambient	OUA + NIT		B[ND] D							
		4d Bound	EPA +OUA + NIT (5-14)	EPA (5-14)	5uM	Ambient	OUA + NIT		NC							
		4d Bound	EPA+Bay +NIT (5-14)	STD+Bay +NiIT	5uM	Ambient	BAY + NIT		B[ND] D							
		4d Bound	EPA+Bay +NIT (5-14)	EPA (5-14)	5uM	Ambient	BAY + NIT		NC							

Table 3-28. Effects of Omega-3 Fatty Acids on Ion Pumps and Ion Movement in Isolated Organ and Cell Culture Studies

Author, Year	Model [Animal, Type, Age]	Exposure Duration	Comparison Groups		Amount of Omega-3	Experimental Condition	Agent	Pump Activity	Cys. Ca^{2+} influx	Cys. Ca^{2+} efflux	Cys Ca^{2+} Content	SR Ca^{2+} Content	SR Ca^{2+} Uptake	SR Ca^{2+} Release	Exchanger	Other
			Omega-3 Fatty Acid (n)	Control (n)												
Rodrigo, 1999	Guinea pig, adult, SSP ventricular	10 min Free	EPA (5)	STD (5)	5uM	Ambient	Ca^{2+}							D*		
DOG																
Philipson, 1985	Dog, adult, ventricular SR vesicles	1.5 sec Free	ALA (9)	STD (9)	30uM	Ambient	Ca^{2+}								I* NaCa exchange	
		2 min Free	ALA (3)	STD (3)	20uM	Ambient	Pre-loaded Ca^{2+}									I* SL pass Ca efflux
Philipson, 1987	Dog, adult, ventricular SR vesicles	1.5 sec Free	ALA (3)	STD (3)	60uM	Ambient	Ca^{2+}								I* NaCa exchange	
		2 min Free	ALA (4)	STD (4)	30uM	Ambient	Pre-loaded Ca^{2+}									I* SL pass Ca efflux
Goel, 2002	Pig, adult ventricular SR vesicles	90+/-30s Free	ALA (3-5)	STD (3-5)	50uM	Ambient	None								NC Na/H exchange	
			DHA (3-5)	STD (3-4)	50uM	Ambient	Na^{+}								D* Na/H exchange	
			EPA (3-5)	STD (3-5)	10uM	Ambient	None								NC Na/H exchange	
			EPA (3-5)	STD (3-5)	25uM	Ambient	None								NC Na/H exchange	
			EPA (3-6)	STD (3-6)	50uM	Ambient	None								D* Na/H exchaange	NC pass NA efflux
			EPA (3-5)	STD (3-5)	100uM	Ambient	None								D* Na/H exchaange	
			DHA (3-5)	STD (3-5)	10uM	Ambient	None								NC Na/H exchange	
			DHA (3-5)	STD (3-5)	25uM	Ambient	None								D* Na/H exchange	

Table 3-28. Effects of Omega-3 Fatty Acids on Ion Pumps and Ion Movement in Isolated Organ and Cell Culture Studies

Author, Year	Model [Animal, Type, Age]	Exposure Duration	Comparison Groups		Amount of Omega-3	Experimental Condition	Agent	Pump Activity	Cys. Ca^{2+} influx	Cys. Ca^{2+} efflux	Cys Ca^{2+} Content	SR Ca^{2+} Content	SR Ca^{2+} Uptake	SR Ca^{2+} Release	Exchanger	Other
			Omega-3 Fatty Acid (n)	Control (n)												
			DHA (3-5)	STD (3-5)	50uM	Ambient	None								D*$_{Na/H}$ exchange	NC$_{pass}$ NA efflux
			DHA (3-5)	STD (3-5)	100uM	Ambient	None								D*$_{Na/H}$ exchange	

Cys= cytopsolic; SR= sarcoplasmic reticulum; D = decrease; I = increase; NC = no change; ND= no data; * = p<0.05 ** = p<0.01; *** = p<0.001

ALA =alpha linoleic acud
B =blocked
Bas =baseline
BAY = Bay K8644
BUME =bumetamide
Caff =caffeine
D = decrease
DHA =decosahexaenoic acid
DXR =doxorubicin
EPA =eicosapentaenoic acid
ET-1 =endothelin-1
I =increased
ISO =isoproteronol
KCI =potassium chloride
KRB =Krebs Ringer bicarbonate
LPC =lysophosphatidylcholine
Na =sodium
Na/K =sodium/potassium
NC =no change
ND =no data
NIT =nitrendipine
OUA =ouabain
SL =sarcolemma
SR =sarcoplasmic reticulum
STD = standard chow
uM =micromoles

Table 3-29. Effects of Omega-3 Fatty Acids on Ion Currents in Isolated Organ and Cell Culture Studies

Author, Year	Model [Animal, Type, Age]	Exposure Duration	Comparison Groups		Amount of Omega-3	Experi-mental Condition	Agent	I_{Na}	I_{to}	I_{CaL}	I_K	I_{KI}	I_{KUR}
			Omega-3 Fatty Acid (n)	Control (n)									
MOUSE													
Honore, 1994	Mouse, neonatal, ventricular	ND Free	DHA (9)	STD (9)	30uM	Ambient	None					NC	D*
RAT													
Bogdanov, 1998	Rat, adult ventricular	3-12 min Free	EPA (4)	STD (4)	5-10uM	Ambient	None						NC
			EPA (4)	STD (4)	20uM	Ambient	None						D*
			EPA (4)	STD (4)	50uM	Ambient	None		D*			NC	D*
			DHA (ND)	STD (ND)	5uM	Ambient	None		D^{ND} D^{ND} A I^{ND} delay D** t				
			DHA (ND)	STD (ND)	5uM	Ambient	INDO		D^{ND} D^{ND} A I^{ND} delay D** t				
			DHA (ND)	STD (ND)	50uM	Ambient	None					NC	D^{ND}
Leifert, 1999	Rat, adult ventricular	4 min Free	ALA (6)	STD (6)	25uM	Ambient	None None	+ve Ac*** -ve InAc**					
			EPA (10)	STD (10)	25uM	Ambient	None	+ve Ac*** -ve InAc**					
			DHA (7)	STD (7)	25uM	Ambient	None	D^{ND} A +ve Ac** -ve InAc**					
Macleod, 1998	Rat, adult ventricular	5 min Free	EPA (6-8)	STD (6-8)	5,10,20uM	Ambient	None	D^{ND} A dd		D^{ND} dd			
			EPA (5-8)	STD (5-8)	0.1-10uM	Ambient	None		D^{ND} dd				
			EPA (ND)	STD (ND)	2uM	Ambient	None				D^{ND}	D^{ND}	
			EPA (ND)	STD (ND)	5uM	Ambient	None				D^{ND}	D^{ND}	
			DHA (6-8)	STD (6-8)	5,10,20uM	Ambient	None	D^{ND} A dd					

Table 3-29. Effects of Omega-3 Fatty Acids on Ion Currents in Isolated Organ and Cell Culture Studies

Author, Year	Model [Animal, Type, Age]	Exposure Duration	Comparison Groups		Amount of Omega-3	Experi-mental Condition	Agent	I_{Na}	I_{to}	I_{CaL}	I_K	I_{KI}	I_{KUR}
			Omega-3 Fatty Acid (n)	Control (n)									
			DHA (5-8)	STD (5-8)	5,7.5,10uM	Ambient	None			D^{ND} dd			
			DHA (5-8)	STD (5-8)	0.1-10uM	Ambient	None		D^{ND} dd				
Negretti, 2000	Rat, adult, ventricular	3 min Free	EPA (5)	STD (5)	10uM	Ambient	None			D* A			
			DHA (5)	STD (5)	10uM	Ambient	None			D* A			
O'Neill, 2002	Rat, ND ventricular	ND Free	EPA (6)	STD (6)	10uM	Ambient	Ca^{2+}		D***F I***A				
Pepe, 1994	Rat, adult, cardiac	4 min Free	DHA (6/gp)	STD (6/gp)	5uM	Ambient	None			NC A			
			DHA (6/gp)	STD (6/gp)	5uM	Ambient	NIT			I* A			
			DHA (6/gp)	STD (6/gp)	5uM	Ambient	BAY			B* A			
			DHA (6/gp)	STD (6/gp)	5uM	Ambient	ISO			NC A			
Rodrigo, 1999	Rat, adult ventricular	10 min Free	EPA (8)	STD (8)	5uM	Ambient	None			D***			
Xiao, 1995	Rat, neonatal, ventricular	ND Free	ALA (5)	STD (5)	10uM	Ambient	None	D*					
			EPA (6-10)	STD (6-10)	5-10uM	Ambient	None	D* NC IVC NC Ac NC InAc					
			EPA (4-10)	STD (4-10)	10-40uM	Ambient	None	D* dd					
			EPA (10)	STD (10)	5-10uM	Ambient	None	D** tdv dependent					
			EPA (21)	STD (21)	10uM	Ambient	None	D***					
			DHA (7)	STD (7)	10uM	Ambient	None	D*					
			DHA (7)	STD (7)	5uM	Ambient	None	D**					
Xiao, 1997	Rat, neonatal, ventricular	ND Free	ALA (5)	STD (5)	5uM	Ambient	None			D** -ve IAC			

Table 3-29. Effects of Omega-3 Fatty Acids on Ion Currents in Isolated Organ and Cell Culture Studies

Author, Year	Model [Animal, Type, Age]	Exposure Duration	Comparison Groups		Amount of Omega-3	Experi-mental Condition	Agent	I_{Na}	I_{to}	I_{CaL}	I_K	I_{KI}	I_{KUR}
			Omega-3 Fatty Acid (n)	Control (n)									
		ND Free	EPA (ND)	STD (ND)	0.1-40uM	Ambient	None			D* dd tdv dependent			
		ND Free	EPA (5)	STD (5)	5uM	Ambient	None			D** -ve IAC			
		ND Free	DHA (6)	STD (6)	5uM	Ambient	None			D** -ve IAC			
		ND Free	EPA (11)	STD (11)	1.5uM	Ambient	None			D* NC IVC -ve Shift IAC			
		ND Free	EPA (5)	STD (5)	1uM	Ambient	None			D**			
		ND Free	EPA (8)	STD (8)	5uM	Ambient	None			D**			
GUINEA PIG													
Ferrier, 2002	Guinea pig, adult, ventricular	20 min Free	DHAm.e (18-24)	STD (18-24)	10uM	Ambient	None			I**			
Macleod, 1998	Guinea pig adult, ventricular	5 min Free	EPA (8-10)	STD (8-10)	5,10,20uM	Ambient	None	D^{ND} A dd					
			EPA (5-8)	STD (5-8)	2, 5uM	Ambient	None				D^{ND}	D^{ND}	
			EPA (5-8)	STD (5-8)	5,7.5,10uM	Ambient	None			D^{ND} A dd			
			DHA (8-10)	STD (8-10)	5,10,20uM	Ambient	None	D^{ND} A dd					
			DHA (6-10)	STD (6-10)	5, 7.5, 10uM	Ambient	None			D^{ND} dd			
Rodrigo, 1999	Guinea pig, adult, ventricular	10 min Free	EPA (11)	STD (11)	5uM	Ambient	None			D***			
FERRET													
Xiao, 2002	Ferret, adult, ventricular	ND Free	ALA (7)	STD (7)	5uM	Ambient	None				D**		
			ALA (4-8)	STD (4-8)	10uM	Ambient	None		D*		D***	NC	
			EPA (6)	STD (6)	5uM	Ambient	None				D*		

Table 3-29. Effects of Omega-3 Fatty Acids on Ion Currents in Isolated Organ and Cell Culture Studies

Author, Year	Model [Animal, Type, Age]	Exposure Duration	Comparison Groups		Amount of Omega-3	Experi-mental Condition	Agent	I_{Na}	I_{to}	I_{CaL}	I_K	I_{Kl}	I_{KUR}
			Omega-3 Fatty Acid (n)	Control (n)									
			EPA (4-8)	STD (4-8)	10uM	Ambient	None		D**		D***	NC	
			DHA (7-12)	STD (7-12)	10uM	Ambient	None				D*		
			DHA (6)	STD (6)	0.2-50uM	Ambient	None				D*dd		
			DHA (6-12)	STD (12)	5uM	Ambient	None				D*	NC	
			DHA (5-8)	STD (5-8)	10uM	Ambient	None		D***		D*	NC	
			DHA (5)	STD (5)	10uM	Ambient	Sta				D*		
			DHA (2-6)	STD (2-6)	20uM	Ambient	None				D**	NC	
			DHA (11)	STD (11)	50uM	Ambient	None				D***		

INA= sodium current; ITO= transient K+ outward current or initial outward current; ICA.L= voltage dependent L-type calcium current/inward calcium current/calcium sparks; IK=delayed rectifier K+ current; IKl= inward recitifer K+ current or tail current; IKUR= ultra rapid K+ current; D = decrease; I = increase; NC = no change; ND= no data;
* = p<0.05 ** = p<0.01; *** = p<0.001

A =amplitude
Ac =activation parameter
ALA =alpha linoleic acid
BAY =Bay K8644
D = decrease
dd =dose dependent
DHA =decosahexaenoic acid
D^{nd} =
EPA =eicosapentaenoic acid
F =frequency
I =increased
IAC =
InAc =inactivation parameter
I^{nd} =
INDO =indomethacin
ISO =isoproteronol
IVC =
NC =no change
ND =no data
NIT =nitrendipine
Sta =standard
STD = standard chow
tdv =
uM =micromoles

Table 3-30. Effects of Omega-3 Fatty Acids on Ion Channels in Isolated Organ and Cell Culture Studies

Author, Year	Model [Animal, Age, Type]	Exposure Duration: Free or Bound	Omega-3 Fatty Acid (n)	Con-trol (n)	Amount of Omega-3	Experi-mental Condition	Agent	Na^+ Channel	Cloned Kv1.5 K+ channels	Nitrendipine Binding To Putative Dihydropyridine Sensitive Ca2+ Channels
MOUSE										
Honore, 1994	Mouse, neonatal, ventricular	ND Free	DHA (5-11)	STD (5-11)	30uM	Ambient	None		B* activity	
			ALA (ND)	STD (ND)	ND	Ambient	None		NC activity	
RAT										
Hallaq, 1992	Rat, neonatal, ventricular	4 d Bound	EPA (5-10)	STD (5-10)	5uM	Ambient	NIT			D* High Affinity K_d D** High Affinity B_{max} D** Low Affinity K_d D* Low Affinity B_{max}
			DHA (5-10)	STD (5-10)	5uM	Ambient	NIT			D** High Affinity K_d D* High Affinity B_{max} D** Low Affinity K_d D* Low Affinity B_{max}
Kang, 1997	Rat, neonatal cardiac	2-3 d Bound	EPA (4)	STD (4)	20uM	Ambient	None	NC in number		
			EPA (4)	STD (4)	20uM	Ambient	MEX	D* in number B* increase in expression		

B= Block; STD=Control; D=decrease; d=days; I= Increase; NC=No change; ND=No data; NIT= Nitrendipine;
MEX= Mexiletine; D = decrease; I = increase; NC = no change; ND= no data; * = $p<0.05$ ** = $p<0.01$; *** = $p<0.001$

B =blocked
Bmax =binding capacity
D = decrease
DHA =decosahexaenoic acid
EPA =eicosapantaenoic acid
Kd =affinity
NC =no change
ND =no data
NIT =nitrendipine
MEX =mexiletine
uM =micromoles
STD =standard

Table 3-31. Comparison of IC50 or EC50 Values in Isolated Organ and Cell Culture Studies

Author, year	Model [Animal, Age, Type]	Exposure Duration	Omega-3 Fatty Acid (n)	Con-trol (n)	Experi-mental Condition	Agent	I_{Na}	I_{to}	I_{CaL}	I_K	TS
Leifert, 1999	Rat, adult, ventricular	4 mins Free	DHA	STD	Ambient	None	6.0 ± 1.2 µM				
			EPA	STD	Ambient	None	16.2 ± 1.3 µM				
			ALA	STD	Ambient	None	26.6 ± 1.3 µM				
Macleod, 1998	Rat, adult, ventricular	5 mins Free	DHA	STD	Ambient	None	12.8 ± 0.8 µM	2.6 ± 0.7 µM	27.9 ± 2.5 µM		63 ± 8.3 µM
			EPA	STD	Ambient	None	7.9 ± 0.6 µM	1.9 ± 0.3 µM	9.4 ± 0.8 µM		51 ± 5.0 µM
	Guinea pig, adult, ventricular	5 mins Free	DHA	STD	Ambient	None	15.7 ± 0.9 µM	34.7 ± 2.6 µM			8.5 ± 1.1 µM
			EPA	STD	Ambient	None	8.9 ± 0.5 µM	8.6 ± 1.5 µM			6.7 ± 2.2 µM
Xiao, 1997	Rat, adult, ventricular	ND Free	EPA	STD	Ambient	None			2.1 µM		
	Rat, neonatal, ventricular	ND Free	EPA	STD	Ambient	None			0.8 µM		
Xiao, 2002	Ferret,adult, ventricular	3min Free	DHA	STD	Ambient	None		7.5 µM		20 µM	

D = decrease; I = increase; NC = no change; ND= no data; * = $p<0.05$ ** = $p<0.01$; *** = $p<0.001$

DHA = decosahexaenoic acid
EPA = eicosapantaenoic acid
ND = no data
STD = standard chow
TS =twitch size
uM =micromoles