Index

A
Abciximab, GpIIb/IIIa inhibition trials, 111, 112
ACE inhibitors, see Angiotensin-converting enzyme inhibitors
N-Acetyl cysteine (NAC), antioxidant activity, 55
Adenovirus vector, gene therapy, 352, 353, 411
Adhesion molecules,
  atherosclerosis role, 89
  inhibitors, 93, 94
  ischemia-reperfusion injury role, 92
  P-selectin expression in platelet activation, 115
β-Adrenergic receptor, gene therapy for signaling modulation, 356–359
AF, see Atrial fibrillation
Alindine, development and mechanism of action, 34, 35
Amiloride, NHE-1 inhibition and clinical trials, 129
Amiodarone,
  atrial fibrillation treatment, 170
  mixed ion channel blocker development, 188
Angiogenesis therapy,
  assessment of therapeutic benefit, 413–415
  delivery of agents, 410, 411
  fibroblast growth factor, 409, 411
  historical perspective, 407, 408
  master switch genes, 410
  patient selection, 412, 413
  placebo effect, 415
  platelet-derived growth factor, 409
  prospects, 416
  vascular endothelial growth factor, 409–411
Angiotensin II,
  pharmacometrics in receptor antagonist development, 379–385
  ventricular fibrillation role and therapeutic targeting, 211, 212
Angiotensin-converting enzyme (ACE) inhibitors, mitogen-activated protein kinase signaling effects, 77
Antiarrhythmic drugs,
  animal studies, arrhythmia induction, 14, 15
  classification, 178, 186, 187
  costs of development, 365, 366
  history of development, 3–5
  market potential, 3, 4
Arginine, antioxidant activity, 54
Arrhythmogenic right ventricular dysplasia/cardiomyopathy (ARVD/C),
  Brugada syndrome association, 337, 338
  clinical features, 335
  gene mutations, 335–337
  pathology, 318
Atherosclerosis,
  angiogenesis therapy, see Angiogenesis therapy
  inflammation role,
    adhesion molecules, 89
    cytokines, 88, 89
    monocytes, 89, 90
    overview, 88
    plaque instability, 90
    therapeutic targeting, 91
  nitric oxide and endothelial dysfunction in cardiovascular disease, 96, 97
  risk factors, 141, 142
ARVD/C, see Arrhythmogenic right ventricular dysplasia/ cardiomyopathy

Atrial fibrillation (AF),
drug therapy,
amiodarone, 170
CAST trial, 169
classes and mechanisms of action, 169, 170
dofetilide, 170
flecainide, 169
propafenone, 169
prospects, 170, 171
quinidine, 169
RSD1235, 170
sotalol, 170
SWORD trial, 170
ectopic focus, 166
epidemiology, 163
etiology, 163
heart failure patients, 166, 168
history of study, 164
ionic remodeling, 167, 168
membrane potentials and ion channels, 165, 166
multiple wavelet hypothesis, 164
reactive oxygen species role, 171
refractory period duration, 164, 165
stroke risks, 163
structural remodeling and fibrosis, 166, 167
sympathetic induction, 168, 169

B
Beta blockers,
efficacy, 5
ventricular arrhythmia management, 185, 187, 207

Brugada syndrome,
arrhythmogenic right ventricular dysplasia/cardiomyopathy association, 337, 338
clinical features, 329, 330
final common pathway hypothesis, 339, 340
gene mutations, 331
heredity, 330
risk stratification, 331, 332

C
Calcium, gene therapy for homeostasis manipulation, 355, 356
Calcium channel,
auxiliary subunits, 8
cardiac action potential role, 7, 8, 248–250
drug interaction sites, 8
heterologous expression, see Ion channels, heterologous expression
inhibitors, ventricular arrhythmia management, 182, 183
pore-forming subunits, 251–253
structure, 8
cycle-gated channels, 228, 229, 251
CAMP, see Cyclic AMP
CAP, see Cardiac action potential
Cardiac action potential (CAP),
electrocardiogram, 10
ion channel modulation, 5, 7, 8, 247–249
phases, 5–7
Cardiac contractility, antiarrhythmic drug evaluation, 13
Cardiac output, antiarrhythmic drug evaluation, 13
Cardiac pacemaker current, see I(f)
Cardiac pacing, delayed myocardial protection, 279–283
Cardiac troponin,
central laboratory assays, 307–309
chest pain evaluation, 300–305
myocardial infarction criteria, 299–301, 303, 304
point-of-care testing, 309–312
reperfusion assessment, 306, 307
risk assessment in acute coronary syndromes, 304–306
Cardiomyocyte,
antiarrhythmic drug evaluation, 15, 16
apoptosis modulation by nitric oxide, 149
Cariporide, 
mechanism of action, 5 
NHE-1 inhibition and clinical trials,
129, 130, 133, 135, 182 
Carotenoids, antioxidant activity, 54 
Carvedilol, antioxidant activity, 55 
Catecholamines, 
delayed myocardial protection, 272 
ventricular fibrillation role and therapeutic targeting, 207 
CD40 ligand, expression in platelet activation, 115 
CKMB, see Creatine kinase MB 
Clinical trials, 
costs, 21, 365 
design limitations, 366 
endpoints, 21 
pharmacometrics, see Pharmacometrics 
phases, 20, 21 
preclinical studies, 19, 20 
Coenzyme Q10, antioxidant activity, 54 
Conduction disorders, 
dilated cardiomyopathy, 333, 334 
final common pathway hypothesis, 339, 340 
gene mutations, 333 
isolated cardiac conduction disease, 333 
Lev-Lenegre disease, 333, 334 
Congestive heart failure, see Heart failure 
Coronary blood flow, antiarrhythmic drug evaluation, 13 
Creatine kinase MB (CKMB), 
central laboratory assays, 307, 309 
chest pain evaluation, 300–305 
myocardial infarction criteria, 299–301, 303 
point-of-care testing, 309–312 
reperfusion assessment, 306, 307 
risk assessment in acute coronary syndromes, 304–306 
Cyclic AMP (cAMP), 
delayed myocardial protection role, 285, 286 
targeting in ventricular arrhythmia management, 185 
therapeutic application, 287, 288 
D 
Delayed myocardial protection, 
cardiac pacing, 279–283 
chronic hypoxia, 285 
exercise, 283, 284 
heat stress, 284, 285 
history of study, 272 
ischemic preconditioning, 279 
mechanisms, 285–287 
substrates in adaptation, 
catecholamines, 272 
lipopolysaccharide, 275–279 
prostaglandins, 273–275 
therapeutic application, 287, 288 
Desmoplakin, mutations in arrhythmogenic right ventricular dysplasia/ cardiomyopathy, 336, 337 
DNA microarray, high throughput screening, 19 
Dofetilide, atrial fibrillation treatment, 170 
E 
EKG, see Electrocardiography 
Electrocardiography (EKG), antiarrhythmic drug evaluation, 13, 14, 27, 28 
components, 10 
ischemia-induced changes, 9, 10 
myocardial infarction assessment, 298, 299 
species differences, 10, 11 
Electrophysiology, antiarrhythmic drug evaluation, 15, 16 
Endothelin, ventricular fibrillation role and therapeutic targeting, 212 
Eniporide, NHE-1 inhibition and ventricular arrhythmia management, 182 
Eptifibatide, GpIIb/IIIa inhibition trials, 112
Estrogen, myocardial signaling in heart failure, 396–398
supplementation in postmenopausal women, 396
Exercise, delayed myocardial protection, 283, 284
ischemic preconditioning, 149, 150
Extracellular-regulated kinase, see Mitogen-activated protein kinase

F
Falipamil, development and mechanism of action, 35–37
FGF, see Fibroblast growth factor
Fibroblast growth factor (FGF), angiogenesis therapy, 409, 411
Final common pathway hypothesis, arrhythmias and cardiomyopathies, 339, 340
Flavonoids, antioxidant activity, 54
Flecainide, atrial fibrillation treatment, 169
Fluorescence resonance energy transfer (FRET), drug-channel interactions, 240, 241
FRET, see Fluorescence resonance energy transfer

G
Gene therapy, adenovirus vectors, 352, 353, 411
β-adrenergic receptor signaling modulation, 356–359
angiogenesis therapy, 411
antioxidant enzymes, 58
calcium homeostasis manipulation, 355, 356
heart failure, 351, 354, 357–360
ischemic heart disease, 359, 360
myocardial vectors and comparison of vectors, 352–354
transmyocardial laser revascularization, 359
vascular endothelial growth factor, 359, 360
Glibenclamide, mechanism of action, 184
Glutathione, antioxidant activity, 54
GpIIb/IIIa inhibitors, abciximab, 111, 112
clinical trials, CAPTURE, 111, 112
EPILOG, 111, 112
ESPRIT, 112
EXCITE, 113
IMPACT-II, 112
OPUS-TIMI 16, 113
PRISM, 112
PRISM-PLUS, 112
Pursuit, 112
RESTORE, 112
SYMPHONY, 113
eptifibatide, 112
oral antagonists, 113
rational design, 113, 114
restenosis prevention, 96
tirofiban, 112, 113

H
HCN channels, see Hyperpolarization-activated cyclic nucleotide-gated channels
Heart failure, atrial fibrillation, see Atrial fibrillation
economic impact, 389, 390
epidemiology, 389
gene therapy, 351, 354, 357–360, 391
mitogen-activated protein kinase signaling, 71–73
NHE-1 role, 131–134
sex differences, animal model studies, 393–396
estrogen, myocardial signaling, 396–398
supplementation in postmenopausal women, 396
incidence in aging, 391, 392
mortality, 392
pharmacotherapy response, 392
prospects for study, 399, 400
remodeling, 392, 393, 398
selective estrogen receptor
modulator response, 398, 399
Heat shock protein, cardioprotection and
nitric oxide modulation, 148, 149
Heat stress, delayed myocardial
protection, 284, 285
High throughput screening (HTS),
antiiarrhythmic drug development,
17–19
DNA microarrays, 19
fluorescence assays, 18
radiotracer assays, 18
Histamine, ventricular fibrillation role and
therapeutic targeting, 207, 208
HTS, see High throughput screening
Hyperpolarization-activated cyclic
nucleotide-gated (HCN)
channels,
blocker development,
alindine, 34, 35
falipamil, 35–37
ivabradine, 38
side effects, 38
zatebradine, 37, 38
ZD 7288, 35
clinical relevance, 33, 34
gene cloning, 31, 32
nomenclature and types, 31, 32, 38, 39
structure, 32
tissue distribution, 33
Hypertrophy, see Heart failure

I
I(f), see also Hyperpolarization-
activated cyclic nucleotide-
gated channels,
adrenaline effects, 29
hormonal control, 30
pacemaker channel molecular
biology, 30–32
pacemaking role, 28, 29
phosphorylative modulation, 29
variability in different tissues, 30
voltage dependence, 28
IFN-γ, see Interferon-γ
I(h), pacemaker channel molecular
biology, 30–32
IL-1, see Interleukin-1
IL-6, see Interleukin-6
Illoprost, delayed myocardial protection
induction, 274, 275
Interferon-γ (IFN-γ), atherosclerosis
role, 89
Interleukin-1 (IL-1),
atherosclerosis role, 89
ischemia-reperfusion injury role, 91, 92
restenosis role, 95
Interleukin-6 (IL-6), ischemia-
reperfusion injury role, 91, 92
Ion channels, heterologous expression,
assays for drug characterization,
binding assays, 237, 238
electrophysiology, 236, 237
optical assays,
fluorescence resonance energy
transfer of drug-channel
interactions, 240, 241
ion-selective probes, 239, 240
membrane potential indicators,
238, 239
prospects, 241
radioactive ion flux assays, 238
cardiac drug development, overview,
229–231
mammalian cell systems,
advantages, 232, 233
expression vectors, 234
host selection, 233, 234
stable expression, 233, 234
transfection, 234, 235
transient expression, 233
rationale, 229, 230
transgenic animals, 235
Xenopus oocyte system, 232
Ischemia-reperfusion injury,
adhesion molecules, 92
anti-inflammatory therapy, 94
cytokine modulation, 91, 92
ischemia duration and prognosis,
143, 144
mitogen-activated protein kinase signaling, 73, 74, 78
neutrophils and endothelial activation, 92
NHE-1 role, 128, 129
nuclear factor-κB role, 92
reactive oxygen species role, 93, 144, 145
Ischemic preconditioning (PC), animal studies, 145, 146
delayed myocardial protection, 279
everal-phase preconditioning, 146
exercise training benefits, 149, 150
heat shock protein cardioprotection, 147–149
late-phase preconditioning, 146, 147, 152
lipopolysaccharide effects, 150, 151
mitogen-activated protein kinase signaling, 74, 75
nitric oxide modulation, 146–152
Isolated perfused heart, antiarrhythmic drug evaluation, 16
Ivabradine, development and mechanism of action, 38

J
Jun N-terminal kinase, see Mitogen-activated protein kinase

L
Lamifiban, GpIIb/IIIa inhibition trials, 113
Leukotrienes, ventricular fibrillation role and therapeutic targeting, 211
Lev-Lenegre disease, see Conduction disorders
Lipopolysaccharide (LPS), delayed myocardial protection, 275–279
ischemic preconditioning, 150, 151
Long-QT syndrome (LQTS), animal models, 328
clinical features, 318
etiology, 318
familial syndromes, 318
final common pathway hypothesis, 339, 340
genotype-phenotype correlations, clinical features, 327
electrocardiographic features, 327, 328
ion channel mutations, 11, 12, 229, 251, 319–327
Jervell and Lange-Nielson syndrome gene mutations, 326, 327
LQT2 gene mutations, 322, 324
LQT3 gene mutations, 324
LQT5 gene mutations, 324
LQT6 gene mutations, 326
Romano-Ward syndrome gene mutations, 320, 322
treatment, 328, 329
LPC, see Lysophosphatidylcholine
LPS, see Lipopolysaccharide
LQTS, see Long-QT syndrome
Lyso phosphatidylcholine (LPC), ventricular fibrillation role and therapeutic targeting, 209

M
Magnetic resonance imaging (MRI), angiogenesis therapy assessment, 415
MAP, see Monophasic action potential
MAPK, see Mitogen-activated protein kinase
Melatonin, antioxidant activity, 54
MI, see Myocardial infarction
Mitogen-activated protein kinase (MAPK),
cardiac pathology roles, hypertrophy and heart failure, 71–73
ischemia-reperfusion injury, 73, 74, 78
cardioprotection roles, delayed cardioprotection, 75
ischemic preconditioning, 74, 75
inhibitors and therapeutic applications, 76, 77
myocardial regulation, extracellular-regulated kinase pathway activation, 69
p38 pathway activation, 69, 70
stress-activated/Jun N-terminal kinase activation, 70, 71
prospects for therapeutic modulation, 78
signaling cascade, 67
types, 67, 68
MLA, see Monophosphoryl lipid A
Monocyte, atherosclerosis role, 89, 90
Monophasic action potential (MAP), antiarrhythmic drug evaluation, 14
Monophosphoryl lipid A (MLA), delayed myocardial protection induction, 276–278
ischemic preconditioning, 150, 151
MRI, see Magnetic resonance imaging
Myocardial infarction (MI), clinical definition, 299, 300
markers, see Cardiac troponin; Creatine kinase MB; Myoglobin rapid turnaround time assessment, 297, 298
Myoglobin, central laboratory assays, 307, 309
chest pain evaluation, 300–305
myocardial infarction criteria, 299–301, 303
point-of-care testing, 309–312
reperfusion assessment, 306, 307
N
NAC, see N-Acetyl cysteine
Neutrophil, anti-inflammatory therapy, 93, 94
inhibitors, 94
ischemia-reperfusion injury role, 92
restenosis role, 95
NF-κB, see Nuclear factor-κB
NHE, see Sodium-hydrogen exchanger
Nitric oxide (NO), cardiomyocyte apoptosis modulation, 149
endothelial dysfunction in cardiovascular disease, 96, 97
exercise training benefits, 149, 150
functions, 142, 143
heat shock protein modulation, 148, 149
ischemic preconditioning modulation, 146–152
reactive oxygen species interactions, 52, 145
synthase isoforms and synthesis, 96, 142, 143
NO, see Nitric oxide
Nuclear factor-κB (NF-κB), inhibition, 94
ischemia-reperfusion injury role, 92
O
Opioids, ventricular fibrillation role and therapeutic targeting, 212, 213
Orbofiban, GpIIb/IIIa inhibition trials, 113
Oxidative stress, see Reactive oxygen species
P
p38, see Mitogen-activated protein kinase
PAF, see Platelet-activating factor
Palmitoylcarnitine (PC), ventricular fibrillation role and therapeutic targeting, 209
PC, see Ischemic preconditioning; Palmitoylcarnitine
PDGF, see Platelet-derived growth factor
PET, see Positron emission tomography
Pharmacometrics, angiotensin II receptor antagonist development, 379–385
definition, 366
dose-response curves and doe escalation, 375–378
knowledge discovery process, 371–373
learn-confirm-learn approach, 374, 376
models in drug development, 378, 379
outcomes models, 369
pharmacodynamics, 367, 368
pharmacokinetics, 366, 367
planning in drug development process, 373
population models, 369–373
real-time modeling, 373
simulations,
covariate model, 373, 374
execution model, 373, 374
input-output model, 373, 374
Monte Carlo simulation, 373

Plakoglobin, mutations in
arrhythmogenic right ventricular
dysplasia/cardiomyopathy, 336

Platelet,
adhesion,
collagen as adhesive substrate and
platelet agonist, 108, 109
vonWillebrand factor role, 107, 108

CD40 ligand expression in
activation, 115

GPIIb/IIIa in aggregation,
agonists, see GpIIb/IIIa
inhibitors
ligand binding, 109, 110
protein-protein interactions, 110
structure, 109–111
P-selectin expression in activation, 115
restenosis role, 95

Platelet-activating factor (PAF),
ventricular fibrillation role and
therapeutic targeting, 209, 210

Platelet-derived growth factor (PDGF),
angiogenesis therapy, 409

POC testing, see Point-of-care testing
Point-of-care (POC) testing, cardiac
injury markers, 309–312

Polymorphic ventricular tachycardia,
clinical features, 338
final common pathway hypothesis,
339, 340
ryanodine receptor mutations, 338

Positron emission tomography (PET),
angiogenesis therapy
assessment, 415

Potassium, ventricular fibrillation role
and therapeutic targeting, 185, 190, 206

Potassium channel,
blockers as antiarrhythmic drugs, 12,
183, 184

cardiac action potential role, 7–9,
248, 249
drug targeting, 9
heterologous expression, see Ion
channels, heterologous
expression
inwardly-rectifying channels,
genetically-altered mice studies,
260, 261
pore-forming subunits, 253, 255,
260, 261
mutations, see Long-QT syndrome
myocardial currents, 250, 251
types, 9, 229, 246
voltage-gated channels,
accessory subunits, 253, 256
ERG1, studies of genetically-
altered mice, 257, 259, 260
interacting proteins, 256, 257
KCNQ1, studies of genetically-
altered mice, 259, 260, 262
pore-forming subunits, 253, 254, 257
transient channel studies of
genetically-altered mice, 257,
262, 263

Preconditioning, see Ischemic
preconditioning

Propafenone, atrial fibrillation
treatment, 169

Prostaglandins,
delayed myocardial protection, 273–275
ventricular fibrillation role and
therapeutic targeting, 210

Q
Quinidine, atrial fibrillation treatment, 169

R
RC-552, ischemic preconditioning, 151
Reactive oxygen species (ROS),
anti-inflammatory therapy, 57
antioxidant enzymes,
exogenous therapy, 57, 58
gene therapy, 5
cardiac drug toxicity, 58
defense mechanisms, 47, 48, 50, 51
formation, 47, 48
ischemia-reperfusion injury role, 92, 144, 145
metal ion chelation therapy, 56, 57
nitric oxide interactions, 52, 145
pathogenesis roles, 47
producing enzyme modulation, 56
prospects for study, 59
scavengers,
  \(N\)-acetyl cysteine, 55
  arginine, 54
carotenoids, 54
carvedilol, 55
coenzyme Q10, 54
flavonoids, 54
glutathione, 54
melatonin, 54
nutriceuticals, 52–54
vitamin C, 53
vitamin E, 53
signaling, 51, 52
sources, 49, 50
types and chemistry, 48, 49
Restenosis,
  angioplasty, 94
  anti-inflammatory therapy, 96
cytokine modulation, 95
inflammation role, 94–96
neutrophil roles, 95
nitric oxide dysfunction, 97
platelet dysfunction, 95, 96
ROS, see Reactive oxygen species
Roxifiban, GpIIb/IIIa inhibition trials, 113
RSD1235, atrial fibrillation treatment, 170
Ryanodine receptor,
  arrhythmogenic right ventricular
dskeletal/cardiovascular system
muscle mutations, 335
  polymorphic ventricular tachycardia
mutations, 338

S
Safety pharmacology, study design, 12
SCN5A,
  Brugada syndrome mutations, 331
  conduction disorder mutations, 333
long-QT syndrome mutations, 324, 325
sudden infant death syndrome
mutations, 323, 334, 335
Selective estrogen receptor modulators
(SERMs), heart failure response, 398, 399
SERMs, see Selective estrogen receptor
modulators
Serotonin, ventricular fibrillation role and
therapeutic targeting, 208, 209
Sibrafiban, GpIIb/IIIa inhibition trials, 113
SIDS, see Sudden infant death
syndrome
Single photon emission computed
tomography (SPECT),
angiogenesis therapy
assessment, 414, 415
SOD, see Superoxide dismutase
Sodium channel,
  accessory subunits, 340
  blockers as antiarrhythmic drugs, 4, 10
  cardiac action potential role, 7, 247–249
  drug interaction sites, 7, 8
  heterologous expression, see Ion
  channel, heterologous
  expression
mutations in disease, 10, 11, see also
SCN5A
pore-forming subunits, 251
structure, 7
voltage-gated channels, 228, 251
Sodium-hydrogen exchanger (NHE),
cardiac remodeling role, 124
inhibitors, NHE-1,
  amiloride, 129, 132
cardioprotection mechanisms, 124, 129, 130
cariporide, 129, 130, 133, 135, 182
demiporide, 130, 182
GUARDIAN trial, 130, 182
prospects, 134, 135
ventricular arrhythmia
management, 182, 213
isoforms, 123–125
NHE-1,
  ATP regulation, 127
expression regulation, 128
G protein activation, 127, 128
hypertrophy and heart failure role, 131–134
intracellular pH regulation, 124–126
ischemia-reperfusion injury role, 128, 129
localization, 125
paracrine and autocrine factor activation, 126
phosphorylation-dependent regulation, 126, 127
phosphorylation-independent regulation, 127
structure, 125
ventricular fibrillation role, 182, 213
regulation, 123
Sotalol, atrial fibrillation treatment, 170
SPECT, see Single photon emission computed tomography
Sudden cardiac death, see Ventricular arrhythmia, lethal ischemic
Sudden infant death syndrome (SIDS), arrhythmias, 317, 318
definition, 334
epidemiology, 334
etiology, 334
QT prolongation, 334
SCN5A mutations, 323, 334, 335
Superoxide dismutase (SOD), exogenous antioxidant enzyme therapy, 57, 58
gene therapy, 58

T

Thromboxane, ventricular fibrillation role and therapeutic targeting, 210, 211
Tirofiban, GpIIb/IIIa inhibition trials, 112, 113
TMR, see Transmyocardial laser revascularization
TNF-α, see Tumor necrosis factor-α
Transmyocardial laser revascularization (TMR), gene therapy, 359
Troponin, see Cardiac troponin

Tumor necrosis factor-α (TNF-α),
atherosclerosis role, 89
ischemia-reperfusion injury role, 91, 92
restenosis role, 95

V

Vascular endothelial growth factor (VEGF), angiogenesis therapy, 409–411
gene therapy, 359, 360
VEGF, see Vascular endothelial growth factor
Ventricular arrhythmia, lethal ischemic, arrhythmogens, 178
biochemical mediators of arrhythmogenesis and therapeutic targeting,
catecholamines, 207
criteria, 205, 206
endothelin, 212
histamine, 207, 208
leukotrienes, 211
lysophosphatidylcholine, 209
opioids, 212, 213
palmitylcarnitine, 209
platelet-activating factor, 209, 210
potassium, 206
prostaglandins, 210
proton accumulation, 213
serotonin, 208, 209
thrombin, 214
thromboxane, 210, 211
classification of antiarrhythmic drugs, 178, 186
drug development barriers, 175–177
electrophysiology, 177
epidemiology, 176, 317
inhibitor targets,
arrhythmogens,
cyclic AMP, 185
overview, 184
potassium, 185
calcium channels, 182, 183
NHE-1, 182, 213
potassium channels, 183, 184, 187, 188
ischemia-selective drug development, biological screening, 190, 191
efficacy testing against other arrhythmias, 191
overview, 188, 189
pH considerations, 190
potassium elevation, 190
mechanisms of ventricular fibrillation, 204, 205
pathology, 178–180
sudden cardiac death, 203, 317
tachyarrhythmia targeting, 181
targeting of specific arrhythmias, 178–180, 188, 189

Vitamin C,
antioxidant activity, 53
atrial fibrillation prevention, 171

Vitamin E, antioxidant activity, 53

W

Wolff-Parkinson-White syndrome (WPW),
clinical presentation, 338
epidemiology, 338
etiology, 338, 339
gene mutations, 339
WPW, see Wolff-Parkinson-White syndrome

X

Xemilofiban, GpIIb/IIIa inhibition trials, 113

Xenopus oocyte,
antiarrhythmic drug evaluation, 16
ion channels, heterologous expression, 232

Z

Zatebradine,
development and mechanism of action, 37, 38
lung effects, 38
ZD 7288, development and mechanism of action, 35