Index
Pharmacological Reviews
Volume 33
1981

Acetanilide and phenacetin, as metabolic substrates in study of interindirect differences in drug metabolism in man, 98
Acetylcholine
- analytical method for determination of, 99
- botulinum toxin effect on, 170
- metabolism, 178
- synthesis and storage of, 178
- release
- from nonneural tissue, 166
- substances that promote, 178
- system, stable isotope methods for study of, 99
N-Acetylprocainamide, bioavailability of, in man, 93
Acrolein, nonenzymic decomposition product of 4-hydroxy or 6-hydroxy derivative of cyclophosphamide, 109
Actinomycin D free radical, electron spin spectrum of (fig.), 193
Adrenergic agonists, ocular hypertensive effects of, 145
Adrenergic drugs
- antihypertensive efficacy of, 148
- biochemical mode of action of, 140
- extracocular sites of action, 135
- intracocular sites of action, 136
- potential modes of action, 138
- species differences in response to, 146
Adrenergic innervation, species differences, 146
Adrenergic nervous system, role of, in modulation of aqueous humor dynamics, 135
Adrenergic neuron, drugs that alter function of, 143
Adrenoceptor, role of, in modulation of aqueous humor dynamics, 136
Adrenoceptor agonist, effect on intraocular pressure, 138, 141
β-Agonist, relatively selective, 140
Albumin
- association with positively charged inorganic ions, 29
- binding of
c- covalent, examples of, 33
dep oxyzycocorticostrone, progestosterone, and testosterone, 32
ligands to the same region, 45
- positively charged drugs to (table), 20
- specificity, 33
- steroids to, 32
- binding sites of short-, medium-, and long-chain fatty acids, 27
- chemically modified, ligand binding to, 34
- competitive, two ligands to one site (figs.), 46, 47
- conformational changes of, induced by binding of ligands, 41
- conformational fluctuations of, in aqueous solutions, 39
- conformational stability, by ligand binding, 43
- drugs bound to, 30
- endogenous substances bound to (table), 18
- flexibility of, 39
- human
- binding of negatively charged and electrostatic neutral drugs to (table), 19
- binding of salicylate, indomethacin, salsalate, salsalate, salsasalate, tolbutamide, and warfarin, 31
- diuludine bonds of, characteristic pattern, 21
- haemin binding to, 30
- influence of binding of hexyl, octyl, dodecyl sulfate, octyl and dodecyl sulfonate, and dodecaneoane on fluorescence of, 41
- interaction of alkyl ligands and, study by ultraviolet difference spectra, 41
- ligand binding
- locations of, 34
- properties, species differences, 26
- ligands bound to, survey of, 18
- nondefatted, binding of inorganic ions to (table), 20
- position of cysteine residue in, model (fig.), 39
- position of tryptophan residue, model (fig.), 39
- serum
- binding of L-thyroxine, L-tryptophan, octanoate, chlorozepate, piodobenzoate, chloride ions, dodecyl sulfate, and 2,4-dinitrophenol, 27-29
- binding regions of, 26
- scheme for (table), 27
- bovine, 23
- amino acid sequence, model (fig.), 23
- conformational changes due to ligand binding registered by electron spin resonance spectroscopy, 42
- hydrogen-deuterium exchange, 43
- fragments, ligand binding to, 37
- human
- amino acid sequence, model (fig.), 22
- amino acid sequence of (fig.), 21
- bilirubin binding site, 29; (fig.), 30
distances between various locations of (table), 39
variants of, 21
- human and bovine, common structural features, 24
- molecular aspects of ligand binding to, 17
- structural organisation of (fig.), 24
- subdomain structure of (fig.), 25
- structure, in human, serum, 20
Amino acid analysis of botulinum toxin, 161
Amino acid sequence
- bovine serum albumin, model (fig.), 23
- human serum albumin (fig.), 21
- model (fig.), 22
Aminopropylamine, NMR spectroscopy used in study of new metabolite of, 83
1-γ-Aminobutyrate-5-N(1-oxyl-2,2,6,6,-tetramethyl-4-aminopiperidiny)-2,4-dinitrobenzene, constitutional formula, 30
Amiodarone, effect on thyroxine metabolism, 72
Anabolism, 5-fluorouracil, 1; (fig.), 2
Androgens, effect on plasma binding proteins, 57
Angiotensin
- actions on semi-independent variables of circulation (table), 231
- effects on cardiac output, 231
- dependent variables of circulation (fig.), 232
- α-Antagonists, relatively selective, 141
- β-Antagonists, nonselective and relatively selective, 142
Aqueous humor
- dynamics
- adrenergic pharmacology of, 133
- role of adrenergic nervous system and adrenoceptors in modulation of, 135
- formation of, 134
- outflow of, 134
- production, circulation, and drainage of (fig.), 134
Arachidonic acid reaction with nitroso t-buty1 (fig.), 204
- 1-Arilino-8-naphthalene sulfonate, constitutional formula, 30
Clobifibrate, inhibition of hormone binding to plasma proteins, 60
Clonidine
carbon-13 and the mechanism by which heterocyclic ring cleavage occurs during metabolism of, 111
direct stable isotope dilution for quantitative study of metabolism, 92, 93
effect of, on intraocular pressure, 143
pharmacokinetic studies in man, 93
Clostridial infection, specific features of, 158
Clostridium
deuterium oxide metabolism
Clostridium botulinum
bacterial growth and toxin production, 157
clostridial toxemia and toxin production, 156
viral infection of, 156; (fig.), 158
Contractility, effects on cardiac output, 224; (fig.), 225
Compliance, calculation of, 215
Cryptococcus neoformans, fluorocytosine effects on, 10
Cutaneous photosensitization, drug-induced, free radicals in, 205
Cyclophosphamide
deuterium-labelling techniques
mechanism of action studies, 109
metabolic activation studies, 106
investigated with “pseudoracemic” mixtures,” 96
metabolic activation by reverse stable isotope dilution assay, 91
metabolism of (fig.), 91
Cysteine residue, position of, in serum albumin, model (fig.), 39
Cytochrome c reduction by 5-hydroxyindoles and related compounds (table), 190
Deanol
metabolic fate of, 99
Deoxycorticosterone, binding to albumin, 32
Deuterium
biotransformation, mechanistic aspects of, study, 122
isotope effects
biological consequence of, 117
in a microsomal oxygenase system, 114
in meta-hydroxylations of aromatic substrates, 115
on xenobiotics, 115
physicochemical properties of multiply-deuterated compounds, 117
secondary, 115
studies by examining the initial reaction velocities from separate experiments with unlabelled and deuterated substrates, 114
"switching” of metabolic pathways, 117
intermolecular, 114
intramolecular, 114
primary, 1114
isotopic label
disadvantage of, 89
wide use as, 89
-labeled compounds, synthetic procedures for preparation of, 82
-labeled derivatizing reagent tri(deuteromethyl)silyl groups donated to reactive —OH, —NH, and —SH functionalities, 107
-labeled reagents, use, to facilitate elucidation of molecular structure by mass spectrometry, 107
-stereochemical aspects of metabolic reactions investigated by, 107
-labeled techniques
study of enzyme-mediated rearrangement of hydrogen, 118
hydrogen rearrangements during nonenzymatic degradation of drugs, 119
hydrogen rearrangements in biological systems during metabolism, 118
metabolic attack, defining sites of, 106
molecular rearrangements, 117
-toxicity of polycyclic aromatic hydrocarbons, 115
marker in metabolic studies, 104
mechanistic studies, 108
metabolism study of endogeneous compounds, 101
oxide
carcinolytic effect of, 82
production of, on a commercial scale, 81
retention of, in a hydroxylated metabolite, 107
role of, in biosynthesis and metabolism of prostaglandins, 101
toxicity of, 84
Dextropropoxypheine, stable isotopes used to study bioavailability of salt forms of, 94
Diazepam, inhibition of hormone binding to plasma proteins, 60
Diazouracil, inhibitor of dihydrouracil dehydrogenase, 3
Diazoxide
actions on semi-independent variables of circulation (table), 235
effects in heart failure, 239
on cardiac output, 234
on dependent variables of circulation (fig.), 235
partial deuterium exchange on injection of N-methylated derivative into GC-MS system when methanol was used as solvent, 87
2,4-Dichlorophenoxo acetic acid (2,4-D), inhibition of hormone binding to plasma proteins, 59
Dichlorvos, pharmacological activity of metrifonate associated with, 91
Dihydouracil dehydrogenase, role in catabolism of 5-fluorouracil, 3
5α,7α-Dihydroxy-11-oxotetranorprostane-1,16-dioic acid
δ-lactone structure, 88, 91
“open chain” structure, 91
t-butyldimethylsilyl ether applied to assay of, 88
urinary excretion studies, 102
3,4-Dihydroxyphenylacetic acid (DOPAC) quantitative assay by selected ion monitoring, 100
Dimethylnitrosamine, degradation mechanism, 111
Dimethylsulfoxide, methane generation from, 110
Dinitrophenol
binding to human albumin, 28
inhibition of hormone binding to plasma proteins, 59
Dipivalyl epinephrine, effects of, on intraocular pressure, 139
Disopyramide, use, in bioavailability studies, 94
Dobutamine
actions of, on semi-independent variables of circulation (table), 228
effects in heart failure, 239
on cardiac output, 230
on dependent variables of circulation (fig.), 231
Dodecyl sulfate, binding to human albumin, 28
Dopamine
actions of, on semi-independent variables of circulations (table), 228
effects cardiovascular, 230
in heart failure, 239
on dependent variables of circulation (fig.), 231
on intraocular pressure, 139
-synthesis and metabolism, 100
Drugs
antithyroid, effect on thyroxine metabolism, 65
bound to albumin, 30
effects on cardiac output, 226
mechanisms and quantitative assessment of, new model of the circulation, 213
on distribution and metabolism of thyroid hormones, 55
-induced cutaneous photosensitization, free radicals in, 205
interactions, stable isotopes in studies of, 106
metabolism
application of selected ion monitoring GC-MS to studies of, 102
interindividual differences in, 98
isotope cluster technique (or ion doublet, twin ion technique), 102
negatively charged and electrostatic neutral, binding to human serum albumin (table), 19
positively charged, binding to albumin, (table), 20
Electron spin resonance spectroscopy, conformational changes of bo-
Electron spin resonance spectroscopy—continued
vine serum albumin due to ligand binding, 42
Enflurane, metabolic pathways for liberation of fluoride ion, 116
1-Ephedrine, direct stable isotope dilution for quantitative study of
metabolism in man, with [3H] ephedrine as substrate, 92
Epinephrine
actions of, on semi-independent variables of circulation (table), 227
effects
on aqueous formation and outflow, 138
on cardiac output, 226
on dependent variables of circulation (fig.), 229
Estrogens, effect on plasma binding proteins, 57
Ethanol
chiral hydrate and, synergism in producing a CNS depressant effect,
108
free radicals, 196
Fatty acids, short-, medium-, and long-chain, binding sites of, on the
albumin molecule, 27
Fenofenac, inhibition of hormone binding to plasma proteins, 59
Fluorescence spectroscopy, influence of binding of beryll, octyl, dodecyl
sulfate, octyl and dodecyl sulfonate, and dodecanol on fluo-
rescence of human and bovine serum albumin, 41
3-Fluoro-D-alanine, and its 2-deuterated analog, a new antibacterial, 116
Fluorocytosine
antifungal action, biochemical basis for, 10
cytotoxicity of, 11
selective effect on fungal cells, 10
5-Fluorodeoxyuridine monophosphate
interaction with deoxyuridylate, 6
interaction with thymidylate synthetase, 4
kinetics of, 5
Fluoropyrimidines
biochemistry and pharmacokinetics, progress in understanding of, 1
pharmacology of, 1
Fluorouracil
abolism of, 1; (fig.), 2
biological effects on ribosomal RNA production, 6
bolus vs. continuous i.v. infusion of, 11
catabolism of (fig.), 2, 3
effects on RNA synthesis, processing and function, 6
incorporation into RNA, biological consequences of, 6
interaction with methotrexate, 8
interaction with thymidine, focus of intense scrutiny, 8
intraperitoneal, pharmacology of, 13
metabolism of, 2; (table), 1
5-Fluorouracil
pharmacokinetics of, 11; (table), 11
oral, 12
problem in analysis of, 11
RNA effects vs. thymidylate synthetase inhibition, relative impor-
tance of, 7
thymidine effects on pharmacology of (table), 9
4-Formylaminoantipyrine NMR spectroscopy used in study of, 83
Free radicals
drug-induced cutaneous photosensitization, 205
enzymatic
oxidation of xenobiotics (table), 200
reduction of xenobiotics (table), 199
inorganic, 189
metabolites, novel, 189
pathways, in metabolism of xenobiotics, 198
semiquinoneimine, 189
Fungal cells, fluorocytosine effect on, 10

INDEX
analysis, verification of specificity of, 90
assays, specificity of selected ion monitoring, 90
role in development of stable isotope methodology for application to
biological problems, 82
Glucomac
experimentally induced, 147
experimental models of, for pharmacological evaluation (table), 147
Glucocorticoids
effect
on plasma binding proteins, 57
on thyroxine metabolism, 69
Greenway, C. V. Mechanisms and quantitative assessment of drug
effects on cardiac output with a new model of the circulation, 213
Guanethidine, effect of, on intraocular pressure, 144

Haemin, binding to human albumin, 30
Halofenate, inhibition of hormone binding to plasma proteins, 60
Heart failure
alpha-blockers and converting enzyme inhibitors, 238
effects of drugs (fig.), 238
in relation to the Starling function curve, 240
effects on dependent variables (fig.), 237
pressure-volume loops for left ventricle in normal subject and in
patient with heart failure before and after treatment with
nicotinamide (fig.), 240
vasodilators and, 236
Heart rate, effects on cardiac output, 224; (fig.), 225
Heavy water. See Deuterium oxide
Heparin, inhibition of hormone binding to plasma proteins, 60
Heroin, effect on thyroxine metabolism, 63
Hovaanic acid (HVA) quantitative assay by selected ion monitor-
ing, 100
Hormone. See under specific hormone
Human serum albumin. See under Albumin
Hydralazine
actions on semi-independent variables of circulation (table), 233
effects
in heart failure, 239
on cardiac output, 233
on dependent variables of circulation (fig.), 234
-induced lupus erythematosus, 111
Hydrazine derived from metabolism of hydralazine, 111
Hydrogen-deuterium exchange of bovine serum albumin, 43
7α-Hydroxy-5,11-dioxoestrone-proprionate-11,16-diacid
effects of indomethacin, aspirin, or sodium salicylate on, 102
urinary metabolite of PGE2 and PGE2 in man, 87
6-Hydroxydopamine, treatment of refractory glaucoma, 143
5-Hydroxyindoleacetic acid, dopamine and serotonin synthesis by
awake human brain, 100
5-Hydroxyindole
radicals, q-values of, 190; (table), 191
stimulation of NAD(P)H oxidation and oxygen consumption by (fig.),
191
Hypertension, ocular. See Ocular hypertension
Ibuprofen, stereochemical aspects of metabolism, deuterium labelling
in mechanistic studies, 110
Imidazolidinone, cyclic, origin of, in urine of humans and monkeys
given lidocaine, 108
Indomethacin, binding to human albumin, 31
Inhibitor
-enzyme interactions
chemistry of, 4
5-fluorodeoxyuridine monophosphate-thymidylate synthetase, 4
kinetics of, 5
ligand-binding approach, advantages of, 5
catecholamine disposition of, 144
sequential, thymidylate synthesis de novo, 9
uptake, 144

GABA, turnover rate, in rat brain, estimated by 3H-labelled tech-
teiques, 101
GABA-DNB-SL, constitutional formula (fig.), 30
Gas chromatography and mass spectrometry
<table>
<thead>
<tr>
<th>INDEX</th>
</tr>
</thead>
<tbody>
<tr>
<td>deuterium used in study on, 101</td>
</tr>
<tr>
<td>stable isotopes in, 98</td>
</tr>
<tr>
<td>fluorouracil (table), 2</td>
</tr>
<tr>
<td>5-fluorouracil, 1; (fig.), 2</td>
</tr>
<tr>
<td>prostaglandins, role of deuterium in, 101</td>
</tr>
<tr>
<td>thyroxine, agents that alter, 61</td>
</tr>
<tr>
<td>xenobiotics, free radical pathways in, 196</td>
</tr>
<tr>
<td>Metabolites, carbonyl-containing, conversion to corresponding alcohols, 107</td>
</tr>
<tr>
<td>Methadone, effect on thyroxine metabolism, 63</td>
</tr>
<tr>
<td>Methotrexate, interaction of fluorouracil and, 8</td>
</tr>
<tr>
<td>Methoxsalen, pharmacokinetics in humans, 94</td>
</tr>
<tr>
<td>3-Methoxy-4-hydroxyphenylethylene glycol (MHPG), direct method of study of production of, by brain in animals and humans, 100</td>
</tr>
<tr>
<td>N-Methyleneiminium, generation of, from nicotine during metabolic oxidative N-demethylation, 110</td>
</tr>
<tr>
<td>N-methylphenidate, effect on thyroxine metabolism, 63</td>
</tr>
<tr>
<td>α-Methyl-p-tyrosine, effect of, on intraocular pressure, 144</td>
</tr>
<tr>
<td>Metrifonate</td>
</tr>
<tr>
<td>internal standard in biological samples for parent drug in determination of extent of chemical transformation of metrifonate, 90, 91</td>
</tr>
<tr>
<td>pharmacological activity associated with dehydrochlorinated product, dichlorvos, 91</td>
</tr>
<tr>
<td>pharmacokinetics of, in man, 91</td>
</tr>
<tr>
<td>susceptible to chemical transformation, 90</td>
</tr>
<tr>
<td>MHPG, (3-Methoxy-4-sulphophenyl)ethylene glycol</td>
</tr>
<tr>
<td>MMPG sulfate</td>
</tr>
<tr>
<td>[°H]analogue of, synthesis of, 90</td>
</tr>
<tr>
<td>assay procedure with GC-MS and a stable isotope labelled internal standard on grounds of specificity, 90</td>
</tr>
<tr>
<td>Molecular biology</td>
</tr>
<tr>
<td>botulinum toxin and, 179</td>
</tr>
<tr>
<td>nerve ending and, 181</td>
</tr>
<tr>
<td>Molecular rearrangements</td>
</tr>
<tr>
<td>enzyme-mediated, 118</td>
</tr>
<tr>
<td>hydrogen, migrating, origin and ultimate fate of, 118</td>
</tr>
<tr>
<td>Monoamine oxidase, inhibitors of, 144</td>
</tr>
<tr>
<td>Myers, Charles E. The pharmacology of the fluoropyrimidines, 1</td>
</tr>
<tr>
<td>Naphthalene</td>
</tr>
<tr>
<td>isolation of the putative arene oxide of, 112</td>
</tr>
<tr>
<td>metabolism study, with D₂O (fig.), 112</td>
</tr>
<tr>
<td>NAD(P)/H oxidation, stimulation of, by serotonin and other 5-hydroxyindoles (fig.), 191</td>
</tr>
<tr>
<td>Nerve ending, molecular biology and, 181</td>
</tr>
<tr>
<td>Nervous system, adrenergic. See Adrenergic nervous system</td>
</tr>
<tr>
<td>Neurotransmitters, stable isotope techniques applied to study of, 98</td>
</tr>
<tr>
<td>Nicardipine, pharmacokinetics in dogs, 96</td>
</tr>
<tr>
<td>Nicotine, N-methyleneiminium generated during metabolic oxidative N-demethylation, 110</td>
</tr>
<tr>
<td>Nifedipine</td>
</tr>
<tr>
<td>effect</td>
</tr>
<tr>
<td>on cardiac output, 236</td>
</tr>
<tr>
<td>in heart failure, 239</td>
</tr>
<tr>
<td>Nitrogen</td>
</tr>
<tr>
<td>mechanism of oxidation at, oxygen 18 applied to studies on, 112</td>
</tr>
<tr>
<td>Nitrogen-15</td>
</tr>
<tr>
<td>internal standards labelled with, superior, 89</td>
</tr>
<tr>
<td>isotope cluster studies, favored over deuterium, 104</td>
</tr>
<tr>
<td>mechanistic studies, 110</td>
</tr>
<tr>
<td>Nitrogen oxide free radicals, 194</td>
</tr>
<tr>
<td>Nitroglycerin</td>
</tr>
<tr>
<td>actions on semi-independent variables of circulation (table), 235</td>
</tr>
<tr>
<td>effects</td>
</tr>
<tr>
<td>in heart failure, 240</td>
</tr>
<tr>
<td>on cardiac output, 235</td>
</tr>
<tr>
<td>on dependent variables of circulation (fig.), 235</td>
</tr>
<tr>
<td>Nitroprusside</td>
</tr>
<tr>
<td>actions on semi-independent variables of circulation (table), 233</td>
</tr>
</tbody>
</table>
INDEX

Nitroprusside—continued

Nitroso compounds, effect of deuterium substitution on mutagenicity of, 116
Nitrosamine
dehydrogenation, given to rats, analysis of hydrolyses of DNA and RNA isolated from the livers of, 108
effect of deuterium substitution on mutagenicity of, 116
Nitroso compounds, effect of deuterium substitution on mutagenicity of, 116
Nitrosamine
dehydrogenation, given to rats, analysis of hydrolyses of DNA and RNA isolated from the livers of, 108
effect of deuterium substitution on mutagenicity of, 116
Oxidation of, on semi-independent variables of circulation (table), 227
-Oxacyclophosphamide, specific mass spectrometric assays by stable-isotope-labelled internal standards, 91
Oxynorcheline, aromatic hydroxylation of, 96
Oxygen-18
mechanism of oxidation at nitrogen, 112
mechanisms of metabolic oxidation at saturated carbon, 112
mechanistic studies, 111
toxicity of, 85
use of, in investigations of metabolic activation and others, 113
Oxide consumption tracings, before and after addition of arachidonic acid (fig.), 204
Oxygen transfer, mechanism of, by prostaglandin hydroperoxidase, 113
Penicillin, inhibition of hormone binding to plasma proteins, 59
Peroxone radicals, 196
Perphenazine, effect on plasma binding proteins, 58
Pharmacology, free radicals in, 189
Phenacetin acetanilide and, metabolic substrates in study of interindividual differences in drug metabolism in man, 96
conversion to reactive electrophilic intermediates by liver enzymes, 113
Phenobarbital, effect on thyroxine metabolism, 62
Phenoxacyclophosphamide, specific mass spectrometric assays by stable-isotope-labelled internal standards, 91
Phenylbutazone, intermediate in oxidative deamination of amphetamine, 112
Phenylinephrine actions of, on semi-independent variables of circulation (table), 227
effects on intraocular pressure, 139
on cardiac output, 226
on dependent variables of circulation (fig.), 230
3-Phenylpropyl carbamate
metabolic fate in human subjects, 93
urinary metabolites of, studied by isotope cluster technique, 106
Phenyl radical, neutral, 189
Phenylin, effect on thyroxine metabolism, 61
Phosphoramidate
mechanism of, on semi-independent variables of circulation (table), 227
-specific effects on the, 109
-specific mass spectrometric assays by stable-isotope-labelled internal standards, 91
Pitt-Rivers, Rosalind. See Cavaleri and Pitt-Rivers, 55
Potter, David E. Adrenergic pharmacology of aqueous humor dynamics, 133
Procaainamide, kinetics of, 93
Progestrone, binding to albumin, 32
Propoxyphene
deuterium isotope effects, 117
d-[2H2] propoxyphene and, equimolar mixture to show more rapid tissue uptake with levo isomer after oral administration in dogs, 96
metabolic fate in humans, investigation with [benzyl-3H] propoxyphene as substrate, 106
-N-demethylated metabolites of, 106
steady-state pharmacokinetics in dogs, 96
Propranolol
effect on thyroxine metabolism, 67
aromatic hydroxylation, 97
effects of, on intraocular pressure, 141
DL-Propranolol, effect on serum T4, T3, and rT3 in different thyroid states in humans (tables), 69
mechanistic aspects of metabolism investigated by isotope cluster technique, 106
metabolic fate in the dog, 96
metabolism, deuterium labelling in mechanistic studies, 110
Propylthiouracil (PTU)
effect on iodothyronine deiodination in vitro (table), 68
on serum T4 and its derivatives in different thyroid states (table), 66
Prostaglandin bioassay, 111
incorporation of oxygen and nitroso 3-butyl reaction with carbon-centered free radical (fig.), 204
metabolism and, role of stable isotopes, 101
metabolism and, use of deuterium-labelled compounds as internal standards, 86
"carrier" and "internal standard" in quantitative studies with stable-isotope-labelled analogs, 92
endoperoxides, structure of (fig.), 201
hydroperoxidase, mechanism of oxygen transfer by, 113
synthesis incubations, electron spin resonance spectra of (fig.), 203
synthetase, lipoxygenases and, 201
Proteins agents that affect the concentration of plasma binding, 57
plasma, agents that inhibit hormone binding to, 58
plasma binding, of thyroid hormones, 55
tissue binding, in thyroid hormone, 56
"Pseudoracemate" technique
analytical method for study of enantiomeric differences in metabolism and disposition of racemic drugs, 96–97
pitfalls, 97
Radicals, free. See Free radicals
Radiographic contrast media, effect on thyroxine metabolism, 71
Resistance, effect on cardiac output, 224; (fig.), 224
Reverse stable isotope dilution analysis, 85
assay technique, fundamental aspects, 86
assays, for polychlorinated compounds, difficulties encountered, 89
contribution to increased commercial production of organic compounds enriched in deuterium, carbon-13, nitrogen-15, and oxygen-18, 86
principle of, gas chromatography-mass spectrometry assay based on, 86
RNA
fluorouracil effects on synthesis, processing, and function of, 6
INDEX

ribosomal, fluorouracil effects on, 7
Salbutamol, effects in heart failure, 239
Salicylanilides, halogenated, phototoxic and photoallergic responses to, 206
Salicylate
binding to human albumin, 31
inhibition of hormone binding to plasma proteins, 58
SC-27166, antidiarrheal agent, absolute bioavailability studies in rat, dog, and baboon, 94
Serotonin
stimulation of NAD(P)H oxidation and oxygen consumption by (fig.), 191
semiquinoneimine radical electron spin resonance spectrum of (fig.), 190
Serum albumin. See under Albumin
Simpson, Lance L. The origin, structure, and pharmacological activity of botulinum toxin, 155
Sodium nitroprusside, effects on cardiac output, 232
Stable isotope dilution, reverse. See Reverse stable isotope dilution
Stable-isotope labelled analog
alternative approach, when preparation is impractical, 89
"ideal" internal standards, 85
Stable isotope labelled compounds
commercial production of, 84
organic, internal standards usually synthesized in investigator's laboratory, 89
radioisotopic contamination of, 84
Stable isotope-labelled drugs
future use of, 121
increase in use of, 121
advantage of use of, 119

Stable isotopes
analytical techniques
GC-MS, 82
electron spin resonance (ESR) spectroscopy, 84
infrared spectroscopy, 83
mass spectrometry, 82
nuclear magnetic resonance (NMR), 83
selected ion monitoring, 83
applications of
in biochemistry, 81
in biology, 82
in pharmacological research, 82
in toxicology, 82
qualitative, 102
quantitative, 85
atomic masses and natural abundance (table), 84
combined GC-MS, role in development of methodology for application to biological problems, 82
disadvantage of use of, 120
drug interaction studies, 108
expansion of use of, in life sciences, 81
historical account of the discovery of, 81
toxicity of
13C, 15N, 18O, 34S, 85
deuterium, 84
use of, in pharmacological research, 81
Steroids, binding to albumin, 32
Stress, effect on thyroxine metabolism, 70
Structure elucidation of unknown compounds by mass spectrometry, 108
Sulfaethidole, binding to human albumin, 31
Sulfanilamide, phototoxic and photoallergic reactions to, 207
Sulfathiazole, binding to human albumin, 31
Sulfonyleureas, inhibition of hormone binding to plasma proteins, 60
Sulfur oxide free radicals, 195
Terbutaline

[1H4] analog of, synthesized for use as an internal standard, 88
GS-MS assays for, 88
Testosterone
binding to albumin, 32
internal standard in GC-MS assay for plasma testosterone and a metabolic tracer in humans, 102
isotope cluster technique to identify 19-hydroxytestosterone as metabolite of, in human placental microsomes, (fig.), 103
2,3,7,8-Tetrachlorodibenzo-p-dioxin (TCDD), API techniques with 13C-labelled internal standards for determination of, in tissue extracts, 88
Thiyl free radicals, 192
Thymidine
effects on fluorouracil pharmacology (table), 9
interaction with fluorouracil, focus of intense scrutiny, 8
phosphorylase, role in metabolism of 5-fluorouracil, 1
Thymidylylate
sequential inhibition of de novo synthesis of, 9
synthetase, 5-fluorodeoxyuridine monophosphate interaction with, 4
synthetase inhibition, fluorouracil effects on RNA and, relative importance of, 7

Thymoxamine, effect of, on intraocular pressure, 141
Thyroid hormone
agents that affect plasma binding, 57
agents that inhibit binding to plasma proteins, 58
consequences of altered plasma and tissue binding, 56
tissue binding proteins, 56
distribution of, effects of drugs, 55
metabolism of, effects of drugs, 55
plasma binding proteins of, 55
transport of, 55
Thyroxine
agents that alter metabolism of, 61
binding to human serum albumin, 27
Timolol
effects of, on intraocular pressure, 141
use in bioavailability studies, 94
Tolbutamide, binding to human albumin, 31
[4-3H]Toluene, conversion to 4-hydroxy-[3-3H]toluene, by arene oxide pathway (fig.), 118
Toxicology, free radicals in, 189
Toxin
botulinum. See Botulinum toxin
production, bacterial taxonomy and growth of Clostridium botulinum, 156, 157
Triarylmethane dye carbon-centered free radicals, 197
Tri-N,N-dimethyl-anisyl methyl radical electron spin resonance spectrum of (fig.), 197
Trypan blue
binding to 1-anilino-8-naphthalene sulfonic acid (ANS) 29; (fig.), 30
constitutional formula, 30
Tryptophan
binding to human serum albumin, 27
residue, position of, in human albumin, model (fig.), 30
Ultraviolet difference spectroscopy, interaction of alkyl ligands and albumina, 41
Uridine phosphorylase, role in metabolism of 5-fluorouracil, 3
Vanillylmandelic acid, oxidation product of MHPG, 100
Vasodilators, heart failure and, 236
Vasopressin
actions on semi-independent variables of circulation (table), 231
effects on cardiac output, 231
effects on dependent variables of circulation (fig.), 233
Venous system, drug actions on, 225
Viral infection, Clostridium botulinum (fig.), 158
Virus, Clostridium botulinum infected by, 157
Warfarin
  binding to human albumin, 31
  new metabolic pathway for, 106

Xenobiotics
  coadministration of two or more, deuterium-labelling techniques in
defining molecular interactions that result, 108
deuterium isotope effects on, 115

enzyme oxidation of one-electron, 201
enzyme reduction of, 198
metabolism of, free radical pathways in, 198
oxidation of, by enzymatic free radicals (table), 200
reduction of, by enzymatic free radicals (table), 199

Zwitterion, nitrogen-centered, 190
CONTENTS

No. 1, March 1981
Suggestions to Contributors ................................................................. i
The Pharmacology of the Fluoropyrimidines. CHARLES E. MYERS .................. 1
Molecular Aspects of Ligand Binding to Serum Albumin  ULRICH KRAG-HANSEN .... 17
Errata ........................................................................................................ 54

No. 2, June 1981
The Effects of Drugs on the Distribution and Metabolism of Thyroid Hormones. RALPH R.
CAVALIERI and ROSALIND PITT-RIVERS .............................................. 55
The Use of Stable Isotopes in Pharmacological Research. THOMAS A. BAILIE ........ 81

No. 3, September 1981
Adrenergic Pharmacology of Aqueous Humor Dynamics. DAVID E. POTTER ........ 133
The Origin, Structure, and Pharmacological Activity of Botulinum Toxin. LANCE L.
SIMPSON .............................................................................................. 155

No. 4, December 1981
Free Radicals in Pharmacology and Toxicology—Selected Topics. RONALD P. MASON AND
COLIN F. CHIGNELL ............................................................................ 189
Mechanisms and Quantitative Assessment of Drug Effects on Cardiac Output with a New
Model of the Circulation. C. V. GREENWAY ........................................ 213
Index ...................................................................................................... 253
TO AUGMENT YOUR EXPERIENCE—CLINICAL RESOURCES © from WILLIAMS & WILKINS

Let these two exciting titles join forces with your professional abilities.
Try them out free for 20 days!

Manual Of Clinical Pharmacology
Edited by David Robertson, MD, and Craig R. Smith, MD

It is well known that a core armamentarium of several dozen key drugs will suffice for the vast majority of clinical situations. This handy new manual gives you the most thorough understanding possible of the drugs commonly used in clinical practice, and supplies an annotated bibliography on these drugs as a point of access to the more detailed pharmacological literature. The discussion sections are not intended to be complete reviews. They are provided to quickly identify drugs which are practical, difficult, or new. You have to have some knowledge of all of the thousands of drugs on the market ... but you should have a very thorough understanding of the few dozen drugs that are most frequently used. This little book highlights those areas that are truly most important to you.

1981/368 pages/$17.00 (softcover)/7300-1

Practical Clinical Psychopharmacology Second Edition
William S. Appleton, MD and John M. Davis, MD

"The authors, who possess impeccable credentials, have put together a handbook that is reliable, responsible, judicious, careful, and practical."
— from a review of the First Edition in Modern Medicine

The authors call their book "a practical guide based on solid science." You will find it to be an indispensable manual of the latest clinical applications of psychopharmacology.

This new Second Edition distills the essential information from more than 15,000 published articles. It succinctly covers the diverse aspects of psychopharmacology and deals with the major categories of useful pharmaco-therapeutic agents. Practical Clinical Psychopharmacology will provide you with all the latest information so you can prescribe psychotropic drugs rationally and counter side-effects efficiently.

1980/173 pages/illustrated/$15.95/0238-4

ORDER TODAY
YES, please send me these selections on 20-day FREE approval:
- Robertson Manual of Clinical Pharmacology (7300-1) $17.00 [U.S.price]
- Appleton Practical Clinical Psychopharmacology (0238-4) $15.95 [U.S. price]
I've checked the payment option below:
- Payment enclosed. I save all postage and handling with full refund still guaranteed.
- Bill me.
Bill my VISA □ MasterCard □

Residents of CA, VA, MD, please add sales tax. Prices subject to change without notice. Prices slightly higher outside the U.S. Please pay in U.S. dollars.

TO ORDER TOLL FREE, CALL US TODAY at 1-800-638-0672 from 9 AM to 4 PM. From Maryland phones, call 528-4221 collect.

Name
Address
City/State/Zip

7777

Williams & Wilkins Department 363 P.O. Box 1496
Baltimore, Maryland 21203
THE SOURCE.

Stedman's Medical Dictionary
24th Edition

No other medical dictionary has ever compared with Stedman's... and no other Stedman's can be compared with number 24!
Look at these features and compare them to the working dictionary you own now!
- Nearly 100,000 terms with 8,152 new entries and 25,735 revised entries.
- Careful elimination of obsolete, superfluous terms.
- Complete updating of all terms through the end of 1980 by a board of 38 distinguished consultants.
- 518 illustrations, including 93 new and revised drawings and a 24 color-plate Anatomic Atlas.
- "...The best cross-indexing system yet devised." (from a review of the 23rd Edition in ASM NEWS)
- Sturdy hardcover binding and thumb indexed.

1981/1,704 pages/518 illustrations (including 24 color plates)/$33.50

Send me ______ copies of the NEW Stedman's/24 (#7915-8) at $33.50 each.
☐ Payment enclosed (W&W pays shipping)
☐ Bill me (I pay shipping)
☐ VISA ☐ MasterCard

 Residents of CA, VA and MD please add state sales tax. Price slightly higher outside the U.S. Price subject to change without notice. Please pay in U.S. dollars.

name

address

city state zip

Williams & Wilkins
426 East Preston Street, Baltimore, Maryland
21202 USA
266 Fulham Road, London SW10 9EL
England

USE THE COUPON BELOW OR CALL TOLL-FREE
1-800-638-0672 FROM ANYWHERE IN THE U.S. EXCEPT ALASKA AND HAWAII. MARYLAND RESIDENTS CALL COLLECT: 528-4221. WE'LL SEND YOU STEDMAN'S/24 TO EXAMINE FOR 20 DAYS FREE!
Melloni's Illustrated Medical Dictionary

Just published — the ideal medical reference for:
- office
- lab
- clinic
- library

For the person whose job requires knowledge of health science terminology, Melloni's is the reference to turn to. Medical words, definitions, concepts — all are explained clearly and quickly in a unique visual format. Readers get a concise and rapidly comprehended store of knowledge. Retention is improved, too, because with Melloni's they're not just reading a definition, they're seeing it!

One reviewer said, "If a dictionary could ever get on a best seller list, Melloni's should! Readable, interesting format, beautiful illustrations — highly recommended!"

Order today!

1979/532 pages/27,085 entries/2,537 illustrations/$18.95

Williams & Wilkins
Publishers of medical and scientific books for 80 years.

Yes, please send me _______ copy(ies) of the exciting new MELLONI'S ILLUSTRATED MEDICAL DICTIONARY at $18.95 each, on 20-day approval. (If purchased in Maryland, please add 5% sales tax.)

Name
Library
Address

City State Zip

☐ check enclosed ☐ bill me ☐ VISA ☐ MASTER CHARGE

TOLL-FREE TELEPHONE ORDERING: call 1-800-638-0672.
In Maryland call collect: 528-4221.

Williams & Wilkins
Dept. 280 P.O. Box 1496 Baltimore, Maryland 21202
Articles Received for Future Issues

Workshop on Immunological Aspects of Toxicology  
Guest Editors: Edgar Haber and Emil A. Pfitzer

Toward a Neuropsychopharmacology of Habituation: A Vertical Integration  
Arnold J. Mandell and Patrick V. Russo

Immobilized and Insolubilized Drugs, Hormones, and Neurotransmitters: Properties, Mechanisms of Action, and Applications  
J. Craig Venter

Polycyclic Aromatic Compounds and Other Foreign Chemicals  
Olavi Pelkonen and Daniel W. Nebert

The Neuropharmacology of Respiratory Control  
Robert A. Mueller, Dag B. A. Lundberg, George R. Breese, Jan Hedner, Thomas Hedner, and Jan Jonason

Suggestions to Contributors will be found in PHARMACOLOGICAL REVIEWS, 33, i–ii, 1981. Copies may be obtained on request from the new Editor, Dr. James A. Bain, Office of the Executive Associate Dean, School of Medicine, Emory University, 1440 Clifton Road, N.E., Atlanta, Georgia 30322.

The editorial supervision of Pharmacological Reviews is shared jointly with the British Pharmacological Society and the Scandinavian Pharmacological Societies.