

TABLE OF CONTENTS

0. Executive Summary	15
1. Introduction to Virology	17
Introduction.....	17
Virus databases	17
A practical classification of viruses	17
Pathomechanism of viral diseases relevant to therapy	18
Intrinsic host defense against retroviruses	19
Life cycle of virus as basis for antiviral approaches	20
Genetic switch in virus infections	20
Emerging viruses	21
Viral-induced cancer	21
Prophylaxis versus therapy.....	22
Economic impact of viral diseases.....	23
Historical landmarks in the development of antiviral therapies	23
2. Antiviral Approaches.....	25
Classification	25
Antiviral drug discovery and development	25
Viral versus cellular targets for antiviral therapy	25
Antivirals based on double-stranded RNA activated caspase oligomerizer	27
Antimicrobial peptides	27
Immunological approaches	27
Basics of immune regulation in relation to viruses	27
<i>Effect of viruses on the immune system.....</i>	<i>28</i>
<i>Latent viral infections and the immune system</i>	<i>28</i>
Immunomodulating agents.....	29
<i>Amplification of innate immunity</i>	<i>29</i>
<i>Blocking the effects of thromboxane A2 on thromboxane receptor.....</i>	<i>29</i>
<i>Enhancers of immune system</i>	<i>30</i>
<i>Promoting immune-mediated clearance of a chronic viral infections.....</i>	<i>30</i>
<i>Immunoglobulins</i>	<i>30</i>
<i>Bovine lactoferrin.....</i>	<i>31</i>
<i>Quercetin.....</i>	<i>31</i>
Monoclonal antibodies	32
<i>Bavituximab</i>	<i>32</i>
<i>Treatment of viral infection with radiolabeled MAbs</i>	<i>33</i>
<i>Limitations of MAbs and measures to overcome these</i>	<i>33</i>
Interferon-based approaches.....	33
Novel antiviral approaches	34
Squalamine	34
Synthetic modified hypericin compounds.....	34
Targeting Toll-like receptors	34
<i>Potential and drawbacks of TLR-ligands in viral diseases</i>	<i>35</i>
Inhibition of viral transport from cytoplasm into the cell nucleus.....	36
Nitric Oxide based antiviral therapeutics	36
Gene therapy for viral infections.....	36
Antisense approaches to viral infections.....	37
Antisense oligonucleotides	37
Limitations of antisense oligonucleotides as antivirals	38
NEUGENE antisense	38
RNAi.....	38
RNAi screens of viral genomes	39
RNAi for treatment of viral infections	39
Promise and pitfalls of RNAi gene therapy	40
Management of rapidly evolving pathogens	40
Personalized medicine and viral diseases	40
An integrated approach to viral diseases	41
Current problems and needs in antiviral therapy	41
3. Vaccines for Virus Infections	43
Introduction.....	43
Types of vaccines.....	44
Live attenuated virus vaccines	44
DNA vaccines	44
Nanotechnology-based vaccines.....	45
Recombinant viral vaccines	46

Synthetic peptides as vaccines.....	46
Virosomes.....	47
Vaccines based on reverse genetics.....	47
Virus-like particles	47
Routine vaccination in children against viral infections	48
Personalized vaccines	48
Limitations of vaccines	48
Neurological complications of vaccination	49
Expert opinion on antiviral vaccines	49
4. Role of Nanotechnology in Developing Antiviral Agents.....	51
Introduction.....	51
Study of interaction of nanoparticles with viruses.....	51
Nanoparticle antiviral agents	52
Silver nanoparticles.....	52
Fullerenes	52
Nanoviricides	53
Role of micelles in nanopharmaceuticals	53
Some physicochemical characteristics common to polymeric micelles	53
Structure and function of nanoviricides	54
<i>Mechanism of action of NanoViricides</i>	<i>54</i>
<i>Advantages of NanoViricides.....</i>	<i>55</i>
5. Delivery of Antivirals	57
Introduction.....	57
Methods of delivery of antiviral agents	57
Local application of antivirals.....	57
Systemic delivery of of protein-polymer antiviral drugs.....	58
Controlled delivery of antivirals.....	58
Targeted delivery of antivirals	58
Delivery of antivirals to the brain across the blood-brain barrier.....	59
Antiviral vaccine delivery systems	59
Minicell vaccine delivery.....	59
Transnasal delivery of vaccines by Newcastle disease virus as vector	59
Transdermal delivery of vaccines	60
<i>CELLECTRA® electroporation device.....</i>	<i>60</i>
<i>Intramuscular electroporation for delivery of DNA vaccine</i>	<i>60</i>
<i>HIV/AIDS vaccination by transdermal application</i>	<i>60</i>
<i>Transdermal vaccines for influenza</i>	<i>61</i>
Use of nanotechnology for improving delivery of antivirals	61
Macrophage-based nanoformulated antiretroviral therapy	62
Improvement of antiviral vaccine delivery by nanotechnology.....	63
<i>Bacterial spores for delivery of vaccines.....</i>	<i>63</i>
<i>Liposomal antiviral vaccine preparations</i>	<i>63</i>
<i>Nanoparticles for DNA vaccines.....</i>	<i>63</i>
<i>Chitosan-derived nanoparticles for vaccine delivery</i>	<i>64</i>
<i>Use gold nanorods for delivery of RNA immune activator molecules.....</i>	<i>64</i>
<i>Proteosomes™ as vaccine delivery vehicles</i>	<i>64</i>
<i>Polymeric micellae for delivery of DNA vaccine.....</i>	<i>64</i>
<i>"Smart" nanoparticles for delivery of vaccines</i>	<i>65</i>
<i>Nanospheres for controlled release of viral antigens</i>	<i>65</i>
Nanocoating for local viricidal effect	65
Delivery of gene-based antiviral drugs	66
Limitations of delivery of gene, RNAi and antisense therapies	66
Systemic delivery of NanoViricides	66
Concluding remarks on delivery of antiviral agents	67
6. Competitive Assessment of Antiviral Approaches	69
Introduction.....	69
An ideal antiviral agent.....	69
SWOT analysis	69
Concluding remarks	72
7. Influenza Viruses.....	73
Introduction.....	73
Clinical features of influenza.....	73
Colds due to rhinovirus	73
Effects of influenza on the respiratory system.....	74
Effect of avian influenza on the nervous system.....	74
Epidemiology	74

Supermap of avian influenza	74
Influenza A	75
Avian influenza affecting humans	75
Human influenza versus avian influenza	76
H1N1 influenza	77
Immune system and influenza	78
Immune Epitope Database and Analysis Resources	78
Anti-influenza approaches	79
Pharmaceuticals	79
Neuraminidase inhibitors	79
<i>Mechanism of action</i>	79
<i>Tamiflu</i>	80
<i>Zanamivir</i>	80
<i>CS-8958</i>	80
<i>Peramivir</i>	81
<i>Resistance to neuraminidase inhibitors</i>	81
<i>Adverse effects of neuraminidase inhibitors</i>	82
Other drugs for influenza	83
<i>Adamantanes</i>	83
<i>Probenecid</i>	83
Current recommendations for the use of antiviral agents for influenza	83
Vaccines	84
<i>Seasonal influenza vaccines</i>	84
<i>Live attenuated influenza vaccine vs. inactivated vaccine</i>	84
<i>Vaccines for H1N1 influenza</i>	85
Current status of influenza vaccines	86
<i>Current recommendations for influenza vaccination</i>	86
<i>Current status of vaccine preparedness against seasonal influenza</i>	86
<i>Current status of vaccine preparedness against H5N1</i>	87
Limitations, needs and challenges of influenza vaccines	87
<i>Limitations of current influenza vaccines</i>	87
<i>Needs of influenza vaccines</i>	88
<i>Problems with demand and supply of influenza vaccines</i>	89
<i>Problems with access to virus samples</i>	89
<i>FluVac project for development of pandemic influenza vaccine</i>	89
<i>Influenza vaccines for multiple strains of the disease</i>	90
<i>Universal influenza vaccines</i>	90
<i>Future prospects of influenza vaccines</i>	90
Application of new technologies for influenza vaccines	91
<i>Adjuvants</i>	91
<i>Cell culture-derived influenza vaccines</i>	92
<i>DNA vaccines for avian influenza</i>	93
<i>Epitope-based vaccines for influenza</i>	93
<i>Gene-based vaccines for influenza</i>	94
<i>Live attenuated vaccines</i>	94
<i>MAbs for passive immunization against avian influenza</i>	94
<i>M2e-based human influenza A vaccine</i>	94
<i>Pre-pandemic split antigen H5N1 vaccine</i>	95
<i>Recombinant-protein based influenza vaccines</i>	95
<i>Synthetic avian influenza vaccine</i>	96
<i>Viral vectors for influenza vaccination</i>	97
<i>Virus-like particles as influenza vaccines</i>	97
RNAi-based approaches	98
<i>Inhibition of influenza virus by siRNAs</i>	98
<i>Limitations of RNAi approach to influenza</i>	99
<i>Challenges and future prospects of siRNAs for influenza</i>	99
Antisense approaches	100
<i>NEUGENE® antisense for inhibition of multiple strains of influenza A</i>	100
Nanoviricides against influenza	100
Other innovative approaches	101
<i>Abatacept</i>	101
<i>Polymeric coatings to inactivate influenza virus</i>	101
<i>Cytotoxic therapy</i>	101
<i>Cyanovirin</i>	102
<i>Fludase</i>	102
<i>Multiferon®</i>	102
<i>Pyrrolidine dithiocarbamate</i>	103
<i>T-705</i>	103
<i>Value of antivirals in preventing spread of influenza after exposure</i>	103
<i>Resistance to influenza therapy and efforts to overcome it</i>	103
NIAID Centers of Excellence for research on pandemic influenza viruses	104

Research on influenza viruses at Bayer	104
Concluding remarks and future prospects.....	105
8. AIDS/HIV	107
Introduction.....	107
Epidemiology	107
Current concepts of pathomechanisms	107
Decoding the structure of an entire HIV genome	108
Genetic basis of resistance against HIV	108
Host-pathogen interactions that regulate HIV-1 replication.....	108
Pathogenesis of AIDS	109
Visualization of the interaction of HIV-1 proteins with target cells	110
Viral latency in HIV	110
Complications of AIDS	111
AIDS and the nervous system	111
Opportunistic infections in AIDS.....	111
Coexistent HIV-1 and HSV-2	112
Coexistent hepatitis virus infections with HIV.....	112
<i>HIV and HBV</i>	113
<i>HIV and HCV</i>	113
AIDS wasting syndrome.....	114
Current therapies.....	114
Aim of anti-HIV drugs.....	115
Efavirenz	116
Tipranavir	116
Enfuvirtide	117
Darunavir.....	117
Impact of antiretroviral treatment on transmission of HIV	117
Postexposure prophylaxis against HIV	118
Limitations of current therapies.....	119
Adverse effects of antiretroviral therapy	119
Drug resistance in AIDS.....	120
Effect of interruption of HIV treatment.....	121
Reservoirs of HIV Infection.....	121
Persistence of low-level viremia in HIV-1 patients on retroviral therapy	121
Reconsideration of abandoned therapies for AIDS.....	121
Therapies in development.....	121
Drugs in development for HIV/AIDS	122
Nucleoside reverse transcriptase inhibitors	123
<i>Apricitabine</i>	123
Non-nucleoside reverse transcriptase inhibitors	123
<i>Etravirine</i>	123
<i>IDX899</i>	123
Novel protease inhibitors	124
<i>Overcoming HIV-1 resistance to PIs</i>	124
<i>PPL-100</i>	125
Entry inhibitors targeting CCR5 receptor	125
<i>Maraviroc</i>	126
<i>SP-01A</i>	126
<i>MAbs targeting CCR5 receptor</i>	126
<i>PRO 140</i>	127
<i>Ibalizumab</i>	127
Integrase inhibitors	128
<i>Raltegravir (Isentress)</i>	128
<i>Elvitegravir (GS 9137)</i>	129
<i>S/GSK1349572</i>	129
<i>S/GSK1265744</i>	130
Design of fusion inhibitor peptides against enfuvirtide-resistant HIV-1	130
Maturation inhibitors	130
Blocking of pre-integration complex translocation	131
Immune enhancers	131
Pyrimidinediones.....	131
Novel combinations of drugs for prevention of AIDS	132
<i>Truvada</i>	132
<i>Combination of raltegravir, enfuvirtide, and darunavir</i>	132
Other innovative antiviral approaches against HIV/AIDS	132
Enhancing immune response by blockade of PD-1 receptor	132
IL-2 as adjunct to antiretroviral therapy.....	133
A filtration device for HIV-1 as an adjunct to the immune system	133
In vitro evaluation of antiviral drug activity	133
Methods for sustaining antiviral activity	134

Selective targeting of ITK to block multiple steps of HIV replication	134
Drugs from natural sources	134
Anti-HIV activity of drugs that stimulate cholesterol efflux	135
Antiviral hyperactivation-limiting therapeutics	135
Blocking of HIV budding by DC-SIGN protein	135
ATR kinase as a target for anti-HIV drug discovery	136
Nanoviricides for HIV/AIDS	136
Prophylactic measures to prevent HIV infection	136
Microbicial agents for local application in HIV/AIDS	137
<i>Currently investigated microbicials against HIV and their limitations</i>	137
<i>CCR5 receptor blockers</i>	138
<i>P5C-Rantes and recombinant chemokine analogs</i>	138
<i>HIV-1 entry inhibitor griffithsin as a topical microbicide</i>	139
<i>Nanotechnology-based topical microbicides</i>	139
<i>Next generation microbicides for HIV</i>	139
Intracellular immunization in HIV	140
<i>Engineered cellular proteins such as soluble CD4s</i>	140
<i>Intracellular antibodies</i>	140
<i>Selection of T-cell vaccine antigens</i>	140
<i>Glycoprotein 120 as target for neutralizing HIV-1 antibodies</i>	141
<i>Anti-rev single chain antibody fragment</i>	141
Gene therapy strategies in HIV/AIDS	141
<i>Inhibition of HIV-1 replication by lentiviral vectors</i>	142
<i>VRX496 (Lexgenleucel-T)</i>	142
<i>Insertion of protective genes into target cells</i>	143
<i>Use of genes to chemosensitize HIV-1 infected cells</i>	143
<i>Autocrine interferon-β production by somatic cell gene therapy</i>	143
HIV/AIDS vaccines	143
<i>Cell-based vaccines for HIV</i>	144
<i>Delivery of HIV vaccine by an adenoviral vector</i>	145
<i>DNA vaccines for HIV/AIDS</i>	145
<i>Epitope-based DNA vaccines against HIV</i>	146
<i>Gene transfer for HIV vaccination</i>	147
<i>Limitations and needs of HIV vaccines</i>	147
<i>Recombinant HIV proteins</i>	147
<i>Vaccination after discontinuation of antiretroviral treatment</i>	147
Innovations in HIV/AIDS vaccine	148
<i>Attenuated rabies virus-based vaccine for HIV</i>	148
<i>Combination of a prime vaccine and booster vaccine</i>	148
<i>Dendritic cell-based vaccine for HIV</i>	149
<i>DermaVir</i>	149
<i>Early control of HIV by an effector memory T cell vaccine</i>	149
<i>MVA nef vaccine</i>	150
<i>Peptide-based vaccine for HIV</i>	150
<i>Personalized vaccine for HIV</i>	150
<i>Transdermal nanoparticles for immune enhancement in HIV</i>	150
<i>Vaccine to prevent HIV entry at the mucosal level</i>	151
Cell therapy for HIV/AIDS	151
<i>hESCs converted to T-cells for treatment of HIV infection</i>	151
<i>Transplantation of genetically modified hematopoietic cells</i>	152
<i>Transplantation of genetically modified T cells</i>	152
<i>Overlapping Peptide-pulsed Autologous Cells</i>	153
Antisense approaches to AIDS	153
<i>Antisense oligodeoxynucleotides</i>	153
<i>Antisense efforts with PNA constructs</i>	153
<i>RNA decoys</i>	154
<i>Ribozymes</i>	154
RNAi applications in HIV/AIDS	155
<i>A multiple shRNA approach for silencing of HIV-1</i>	155
<i>Aptamer-mediated delivery of anti-HIV siRNAs</i>	156
<i>Bispecific siRNA constructs</i>	156
<i>Role of the nef gene during HIV-1 infection and RNAi</i>	156
<i>siRNA-directed inhibition of HIV-1 infection</i>	157
<i>Synergistic effect of snRNA and siRNA</i>	157
<i>Targeting CXCR4 with siRNAs</i>	158
<i>Targeting CCR5 with siRNAs</i>	158
<i>Concluding remarks on RNAi approach to HIV/AIDS</i>	159
Companies involved in developing gene therapy for HIV/AIDS	159
Conclusions regarding gene therapy of HIV/AIDS	160
Testing for new anti-HIV therapies	160
Personalized approach to management of HIV	160

Differences in response of the body to HIV	161
Variations in action of drugs on HIV	161
<i>Drug-resistance in HIV</i>	161
<i>Replication Capacity measurement</i>	162
<i>Role of biomarkers in management of HIV/AIDS</i>	162
<i>Prevention of adverse reactions to antiviral drugs</i>	162
<i>Nanoviricides as a personalized approach to HIV</i>	163
Concluding remarks and future prospects	163

9. Hepatitis Viruses	165
Introduction	165
Hepatitis delta virus infection	165
Hepatitis A virus infection	165
Hepatitis E virus infection	166
Epidemiology.....	166
Structure of the HEV	166
HEV vaccines.....	166
Epidemiology of HBV	167
Pathogenesis of HBV-induced liver disease	167
Current approaches to management of HBV	168
Entecavir	168
Adefovir dipivoxil	169
Telbivudine	169
Pegylated interferon-alpha	169
Limitations of current therapies and needs of HBV	169
Personalized management of HBV	170
Innovations in the management of HBV	170
Tenofovir disoproxil fumarate	170
Hepatitis B immune globulins	171
<i>Nabi-HB</i>	171
<i>HepaGam B</i>	171
Hepatitis B vaccine composed in a novel nanoemulsion adjuvant	171
Innovative pharmaceuticals for HBV	172
<i>Clevudine</i>	172
<i>HepDirect prodrugs</i>	172
Monoclonal antibodies for HBV.....	173
RNAi-based therapy of HBV	173
Personalized treatment of hepatitis B.....	174
Concluding remarks and future prospects of management of hepatitis B	174
Epidemiology of HCV	174
HCV characteristics	175
Pathomechanism of HCV infection	175
Mechanism of HCV entry	175
HCV and the immune system	175
Mechanism of HCV replication and response to interferon	176
Current approaches to management of HCV	176
Interferon therapy for HCV	176
Limitations of current HCV therapies	177
Novel approaches to HCV	177
HCV protease inhibitors	178
<i>Boceprevir</i>	178
<i>Narlaprevir (SCH 900518)</i>	178
<i>Telaprevir (Incivek)</i>	179
<i>Small molecule HCV protease inhibitors</i>	179
Innovations in interferon therapy for HCV	179
<i>AlbIFN-α2b</i>	180
<i>Directed evolution of gene-shuffled IFN-α for treatment of HCV</i>	180
<i>GEA007.1</i>	180
<i>Omega DUROS</i>	180
<i>PEG-IFN-λ</i>	181
<i>Personalizing interferon therapy of HCV</i>	181
Innovative ribavirin-based treatments	182
<i>Targeted delivery of hemoglobin-ribavirin conjugate for HCV</i>	182
<i>Taribavirin</i>	182
Nucleoside polymerase inhibitor.....	182
<i>Valopicitabine</i>	182
Host cell targets for hepatitis C therapy	183
<i>SP-10</i>	183
NS5a inhibitors	184
Compounds targeting HCV receptor E2	184
Cyclophilin inhibitors	184

<i>Alisporivir</i>	185
Methylene blue	185
Naringenin	185
Nitazoxanide	186
Cyclosporine and analogues as anti-HCV agents	186
Clemizole and HCV	187
RNAi-based approaches to HCV.....	187
<i>Use of adenoviral vectors for RNAi</i>	187
<i>siRNAs for HCV</i>	188
<i>Limitations and drawbacks of siRNA therapy for HCV</i>	188
<i>Role of miRNA in viral infections</i>	189
<i>miR-122 antagonists</i>	189
Therapeutic vaccine for HCV	189
Clinical trials of HCV therapeutics	190
Limitations to the development of effective anti-HCV therapeutics.....	190
<i>Causes of treatment failure in chronic hepatitis C</i>	190
<i>HCV drug resistance</i>	191
Personalized management of HCV infection	191
Role of sequencing in personalized management of HCV	192
Concluding remarks about HCV therapy	193
Future needs in HCV therapy	193
10. Miscellaneous Commercially Important Virus Infections	195
Introduction	195
Herpes viruses	195
Herpes simplex virus	195
Treatment of HSV-1	195
<i>Acyclovir</i>	195
<i>Vaccines for HSV</i>	196
<i>Antisense therapy for HSV-1</i>	196
Herpes simplex virus 2 and genital herpes	196
<i>Famciclovir</i>	197
<i>Intravaginal microbicidal agents for HSV-2</i>	197
<i>Vaccines for HSV-2</i>	197
Herpes simplex keratitis.....	198
Herpes simplex encephalitis	198
Limitations of current HSV therapies.....	199
Herpes zoster virus	199
Herpes zoster and chicken pox	199
Epidemiology of herpes zoster	199
Treatment of herpes zoster	200
Herpes zoster vaccine.....	200
Cytomegalovirus	200
Valganciclovir hydrochloride	201
T-cell therapy for CMV	201
Vaccine for CMV.....	201
Gene therapy of CMV.....	201
Antisense approach to CMV	202
siRNA treatment of CMV.....	202
Epstein-Barr virus	203
Human papilloma virus	203
Epidemiology.....	203
Vaccines for HPV	203
<i>Gardasil</i>	204
<i>Cervarix</i>	204
<i>Vaccine based on fusion proteins of HPV envelope</i>	204
<i>DNA vaccine VGX-3100</i>	205
<i>Limitations of HPV vaccines</i>	205
Antivirals for HPV	206
<i>Imiquimod</i>	206
Novel approaches against HPV	206
<i>Intrabody strategies for the treatment of HPV</i>	206
<i>A novel peptide to inhibit HPV</i>	207
<i>Heat shock protein-based antivirals</i>	207
Respiratory syncytial virus	207
Epidemiology	207
Current management of RSV	208
<i>Palivizumab</i>	208
Innovative anti-RSV products in development.....	208
<i>RSV604</i>	208
<i>MDT-637</i>	208

<i>RNAi approach to RSV</i>	209
Vaccines for RSV	209
<i>BCG as a vaccine against RSV</i>	209
<i>Oral DNA vaccine for RSV</i>	209
Other respiratory viruses	210
Parainfluenzavirus type 3	210
Human metapneumovirus	210
Gastrointestinal viruses	211
Noroviruses	211
Concluding remarks	212
11. Viruses with High Impact but Low Commercial Significance	213
Introduction	213
Chikungunya fever	213
Coxsackie virus	213
Japanese encephalitis	214
Vaccines for JE	214
Parvovirus	215
Polyomavirus JC	215
Rabies	215
Rabies vaccines	216
<i>Recombinant viral vaccines for rabies</i>	216
DNA vaccine against rabies	217
Rabies immune globulin	217
Monoclonal antibodies for rabies	217
NanoViricides approach for rabies	217
The Milwaukee protocol for rabies	218
Rotavirus	218
Epidemiology	218
Vaccines against rotavirus	219
Viral hemorrhagic fevers	219
Dengue	220
<i>Antivirals in development</i>	220
<i>Dengue vaccines</i>	221
<i>Genetic elimination of dengue vector mosquitoes</i>	222
Ebola virus	222
<i>Development of antiviral drugs for Ebola</i>	223
<i>DNA vaccine for Ebola</i>	223
Lassa fever	224
Marburg hemorrhagic fever	224
Yellow fever	225
<i>Vaccines for yellow fever</i>	225
<i>Sequencing of Aedes aegypti genome and control of yellow fever</i>	225
Crimean-Congo hemorrhagic fever	226
West Nile virus	226
Epidemiology	226
Pathogenesis	227
Treatment of West Nile neuroinvasive disease	227
Vaccines against WNV	227
Innovative treatments for WNV	228
Western equine encephalitis	228
Sporadic virus epidemics	228
Coronavirus/severe acute respiratory syndrome	228
<i>Therapeutic approaches to SARS</i>	229
<i>MAbs for SARS</i>	229
<i>siRNA treatment of SARS</i>	230
Zoonotic viral infections	230
Vaccines for zoonotic viral diseases	230
Virus bioterrorism and biowarfare	230
Small pox as a biological weapon	231
<i>Status of small pox vaccination</i>	231
Strategies against virus bioterrorism and biowarfare	232
<i>Increasing resistance by stimulating innate immune mechanisms</i>	232
<i>Nanoviricides for combating viral bioterrorism</i>	232
Concluding remarks	233
12. Markets for Antivirals	235
Introduction	235
Markets according to disease	235
Influenza market	235
HIV/AIDS market	236

Hepatitis B and C markets.....	237
Markets according to products and approaches	237
Market values of monoclonal antibodies for viral diseases	237
Market values of vaccines for viral diseases	237
Markets for vaccines against HPV	238
Markets for other antiviral vaccines	238
Markets according to geographical areas	239
Emerging markets for antiviral therapeutics	239
Geographical distribution of HIV/AIDS market	240
Unmet needs in antivirals	240
Policies regarding conquered viral diseases.....	241
Future of polio vaccine.....	241
Policies concerning HPV vaccine for prevention of cervical cancer	242
<i>HPV vaccine in developing countries</i>	<i>242</i>
Future prospects of innovative approaches.....	243
US Government support of antiviral efforts.....	244
<i>US Government support for R & D in avian influenza vaccines</i>	<i>244</i>
<i>US Government support for developing anti-bioterrorism agents.....</i>	<i>244</i>
The European Union support of antiviral research.....	245
<i>European Commission's research support for anti-HIV/AIDS programs</i>	<i>245</i>
<i>European Commission's support anti-influenza programs</i>	<i>246</i>
Collaboration of biotechnology companies with big pharma	247
Strategies for marketing	247
13. Companies	249
Introduction.....	249
Top companies	249
Profiles of pharmaceutical companies.....	250
Profiles of antiviral companies	266
Profiles of viral vaccine companies	380
Collaborations.....	448
14. References.....	455
Tables	
Table 1-1: A practical classification of viruses.....	17
Table 1-2: Vaccines vs therapeutics for viral diseases.....	23
Table 1-3: Historical landmarks in the development of antiviral therapies	23
Table 2-1: Classification of antiviral strategies	25
Table 2-2: Viral vs cellular targets for discovery of antivirals	26
Table 2-3: Viruses amenable to antisense oligonucleotides.....	37
Table 2-4: Inhibition of viral replication by RNAi	39
Table 3-1: Types of vaccines for viral diseases	44
Table 4-1: Role of nanobiotechnology in virology	51
Table 5-1: Methods of delivery of antiviral agents	57
Table 5-2: Role of nanotechnology for improving delivery of antivirals.....	62
Table 5-3: Commercially available liposomal antiviral vaccines	63
Table 6-1: SWOT of monoclonal antibodies	69
Table 6-2: SWOT of agents that prevention viral entry into cells	70
Table 6-3: SWOT of drugs interfering with intracellular replication	70
Table 6-4: SWOT of protease inhibitors	70
Table 6-5: SWOT of integrase inhibitors.....	70
Table 6-6: SWOT of maturation inhibitors	70
Table 6-7: SWOT of neuraminidase inhibitors	71
Table 6-8: SWOT of targeting Toll-like receptors (TLRs).....	71
Table 6-9: SWOT of topical antivirals agents against viral infections.....	71
Table 6-10: SWOT of gene therapy, antisense oligonucleotides, RNAi.....	71
Table 6-11: SWOT of vaccines	71
Table 6-12: SWOT of NanoViricides.....	72
Table 7-1: Anti-influenza approaches	79
Table 7-2: Antiviral drugs used for influenza	79
Table 7-3: Various approaches to production of influenza vaccines.....	91
Table 8-1: Drugs in clinical development for HIV/AIDS	122
Table 8-2: Strategies for gene therapy of AIDS	141
Table 8-3: Classification of HIV/AIDS vaccines in clinical trials.....	143
Table 8-4: Companies involved in developing gene therapy for HIV/AIDS	159
Table 9-1: Innovations in the treatment of HBV	170
Table 9-2: Innovations for management of HCV	178
Table 9-3: Antiviral agents for HCV targeting host cells	183
Table 9-4: HCV drugs in clinical trials	190
Table 10-1: Methods of delivery of acyclovir.....	195

Table 11-1: Strategies against virus bioterrorism and biowarfare.....	232
Table 12-1: Worldwide market for all antiviral approaches 2011-2021	235
Table 12-2: Markets for antivirals according to virus infections 2011-2021	235
Table 12-3: Markets values of all drugs for HIV/AIDS 2011-2021.....	236
Table 12-4: Market values of monoclonal antibodies for viral diseases 2011-2021.....	237
Table 12-5: Market values of vaccines for viral diseases 2011-2021	238
Table 12-6: Markets for antiviral drugs according to geographical areas 2011-2021	239
Table 12-7: Markets for antiviral vaccines according to geographical areas 2011-2021	239
Table 12-8: Emerging markets for antiviral drugs according to countries 2011-2021	239
Table 12-9: Emerging markets for antiviral vaccines according to countries 2011-2021	240
Table 13-1: Top five antiviral companies.....	249
Table 13-2: Roche antiviral products in development	256
Table 13-3: Collaborations of antiviral companies	448

Figures

Figure 1-1: Varieties of host and cell responses to viral infections	19
Figure 1-2: Cycle of infection and replication of a retrovirus	20
Figure 1-3: Viral-induced cancer	22
Figure 2-1: An integrated approach to viral diseases	41
Figure 4-1: Schematic representation of NanoViricide attacking a virus particle	55
Figure 7-1: Evolution of mutations associated with virulence/drug resistance in H5N1	76
Figure 7-2: Mechanism of development of resistance to oseltamivir	82
Figure 8-1: Mode of action of some current anti-HIV drugs	115
Figure 9-1: Steps of HBV replication and site of action of various drugs	167
Figure 9-2: Omega DUROS device for interferon delivery in chronic hepatitis C.....	181
Figure 12-1: Unmet needs in antivirals	241