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Содержание

М.П.Кирпичников, С.Н.Кочетков		Химия и биомедицина: многообразие и единство целей
С.М.Деев, Е.Н.Лебеденко, Л.Е.Петровская, Д.А.Долгих, А.Г.Габиров, М.П.Кирпичников	1	Неприродные антитела и иммуноконъюгаты с заданными свойствами: оптимизация функций через направленное изменение структуры
Ю.М.Евдокимов, В.И.Саянов, С.Г.Скуридин, Э.В.Штыкова, Н.Г.Хлебцов, Е.И.Кац	27	Физико-химический и нанотехнологический подходы к созданию «твердых» пространственных структур ДНК
Е.С.Северин	43	Новые подходы к избирательной доставке лекарственных препаратов в опухолевые клетки
А.Н.Тевяшова, Е.Н.Олсуфьева, М.Н.Преображенская	61	Создание антибиотиков двойного действия как путь поиска новых перспективных лекарственных препаратов
Л.Н.Рогоза, Н.Ф.Салахутдинов	98	Противоязвенные агенты: химический аспект решения проблемы

Contents

Chemistry and biomedicine: deversity and unity of purposes

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Designed antibodies and immunoconjugates with specified properties: function optimization by structure engineering

1

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Advances and challenges in the field of designed antibodies for clinical application over the last 10–15 years are analyzed. The modular structure of natural antibodies and the prospects for its targeted modification and combination with other structural elements and effector molecules are discussed. The attention is paid to the currently existing methods for engineering of immunoglobulins and prospective strategies for generation and use of monoclonal antibodies, their derivatives and analogues, including abzymes and scaffolds, for diagnosis and targeted therapy of cancer and other socially significant diseases. Bibliography — 225 references.

Physicochemical and nanotechnological approaches to creation of ‘rigid’ spatial structures of DNA

27

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The physicochemical and nanotechnological approaches to construction of ‘rigid’ particles based on double-stranded DNA molecules are considered. The physicochemical methods include cross-linking of adjacent DNA molecules, ordered in quasinematic layers of liquid-crystalline dispersion particles, by synthetic nanobridges consisting of alternating molecules of an antibiotic (daunomycin) and divalent copper ions and cross-linking of these molecules as a result of their salting-out in quasinematic layers of liquid-crystalline dispersion particles under the action of lanthanide cations. The nanotechnological approach is based on insertion of gold nanoparticles into the free space between the double-stranded DNA molecules that form quasinematic layers of liquid-crystalline dispersion particles. This gives rise to extended clusters of gold nanoparticles in the free space and is accompanied by enhancement of the interaction between the DNA molecules *via* gold nanoparticles and by decrease in the solubility of the dispersion particles. These approaches produce integrated ‘rigid’ spatial structures containing DNA molecules that are incompatible with the initial aqueous polymeric solution and have unique properties. Bibliography — 116 references.

New approaches to targeted drug delivery to tumour cells

43

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The key approaches to the creation of targeted drugs to treat human malignant tumours are considered. The stages of development of these approaches are described in detail and theoretically substantiated, and the main results of the experimental work are presented. Considerable attention is given to general characteristics of nanopharmacological agents and to description of the mechanisms of cell interactions with nanodrugs. The scope and limitations of nanodrugs for cancer therapy and for treatment of other diseases are considered. The use of nanodrugs conjugated with vector molecules appears to be the most promising trend of targeted therapy of malignant tumours.

Bibliography — 122 references.

Design of dual action antibiotics as an approach to search for new promising pharmaceutical drugs

61

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The review is devoted to the latest achievements in the design of dual action antibiotics — heterodimeric (chimeric) structures based on antibacterial agents of different classes (fluoroquinolones, anthracyclines, oxazolidines, macrolides and so on). Covalent binding can make the pharmacokinetic characteristics of these molecules more predictable and improve the penetration of each component into the cell. Consequently, not only does the drug efficiency increase owing to inhibition of two targets but also the resistance to one or both antibiotics can be overcome. The theoretical grounds of elaboration, design principles and methods for the synthesis of dual action antibiotics are considered. The structures are classified according to the type of covalent spacer (cleavable or not) connecting the moieties of two agents. Dual action antibiotics with a spacer that can be cleaved in a living cell are considered as dual action prodrugs. Data on the biological action of heterodimeric compounds are presented and structure–activity relationships are analyzed.

Bibliography — 225 references.

Antiulcer agents: chemical aspect of solving the problem

98

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The data published from 1990 to 2013 on the chemical structures and specific activities of compounds active as H_2 -histamine receptor blockers, H^+/K^+ -ATPase inhibitors in the exchange areas of hydrogen ions (proton pump inhibitors) and potassium ions (K^+ -competitive acid blockers) are surveyed. The antisecretory agents with studied cytoprotective activity or with additional therapeutic properties compensating the disorders of internal defence mechanisms are presented. A separate section is devoted to the drugs that prevent or mitigate the NSAID-induced intestine damage. All of the considered structures are classified according to the type of biological mechanism of action. Some aspects of the structure–activity relationships for such compounds are considered.

Bibliography — 83 references.