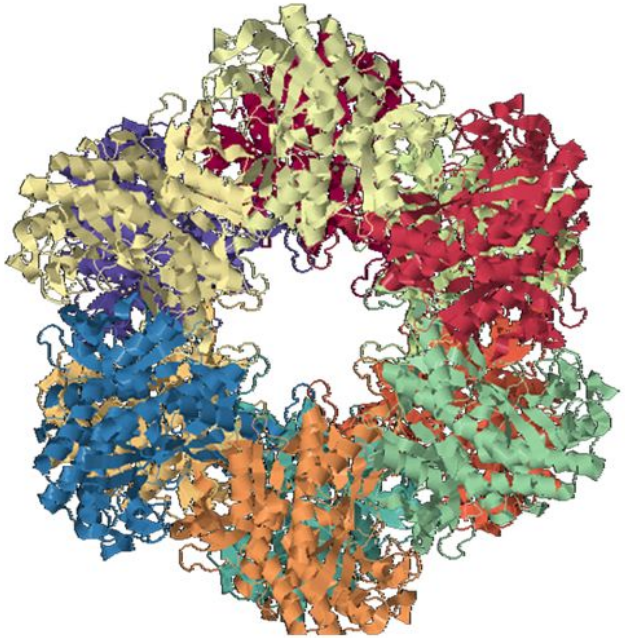
Кружок по медицинской химии

Приглашаем студентов, интересующихся созданием лекарств, на занятия кружка по медицинской химии!



Пятое занятие 03 апреля в 18:30 в 411.

Ждём Вас!

Подробная информация:

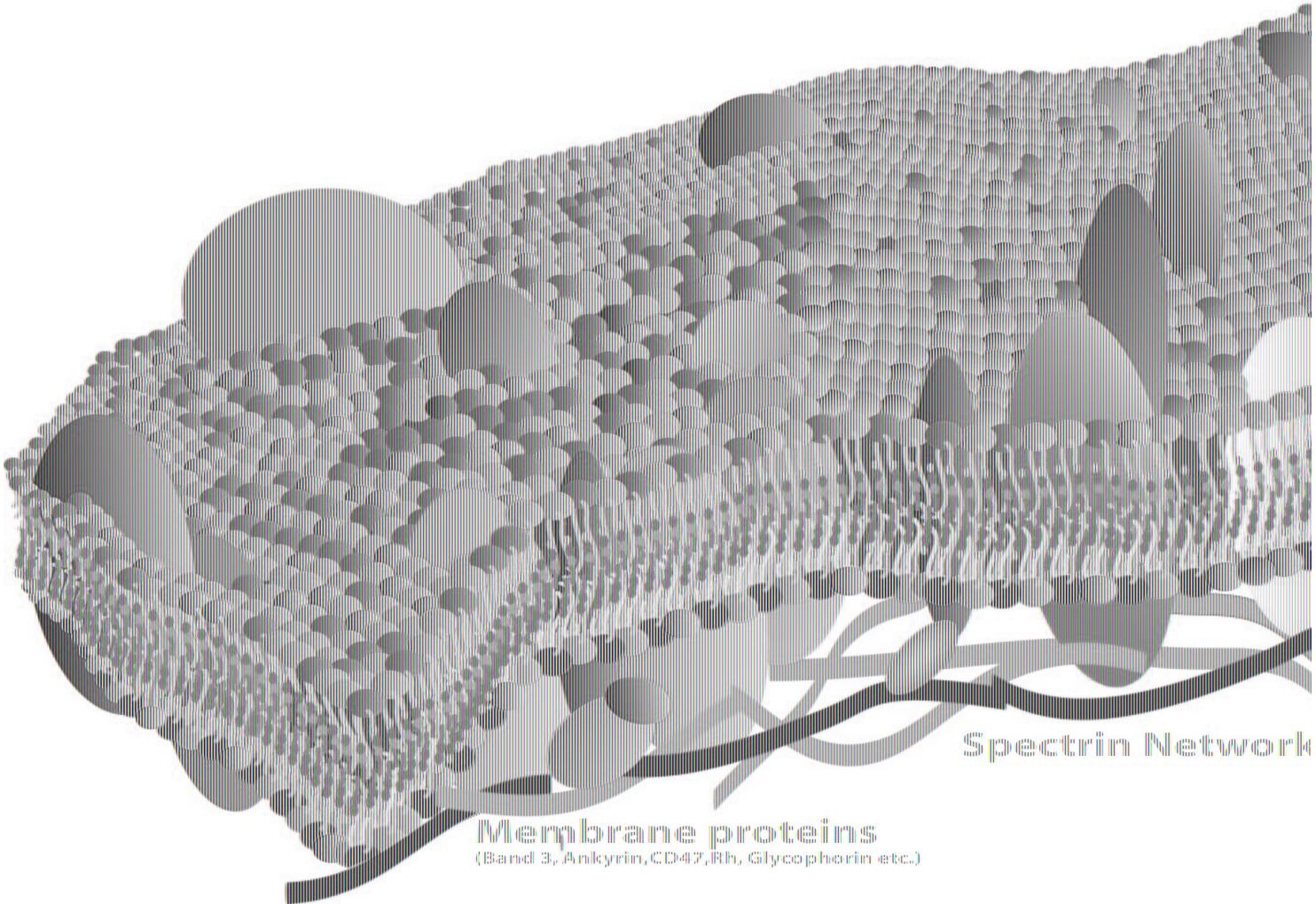
rnase@qsar.chem.msu.ru

http://qsar.chem.msu.ru/ru/obrazov/kruzhok

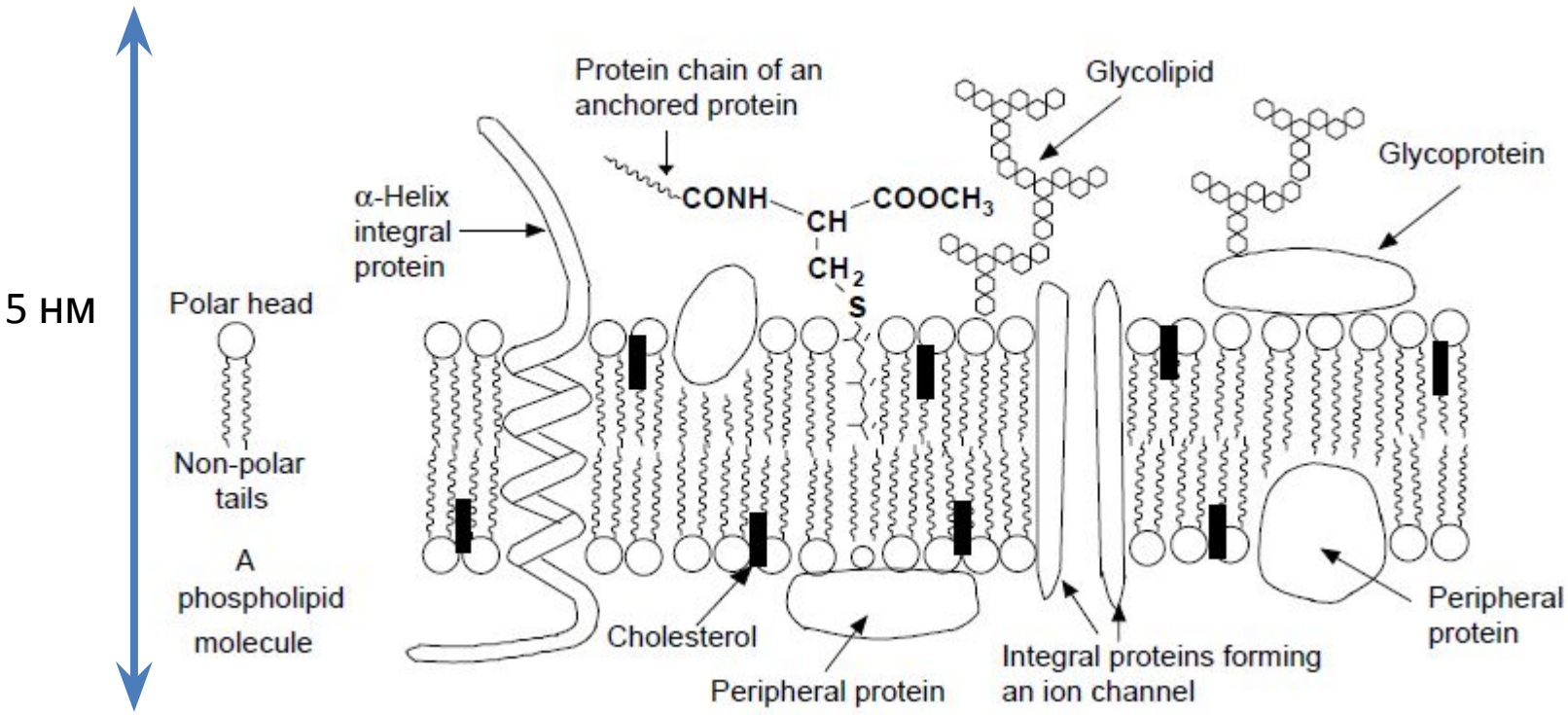
http://goo.gl/UCM8s0

Занятие 5

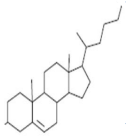
Вещества, действующие на мембрану клетки и клеточную стенку



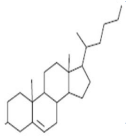
Строение мембраны



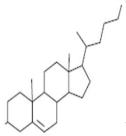
Состав мембраны



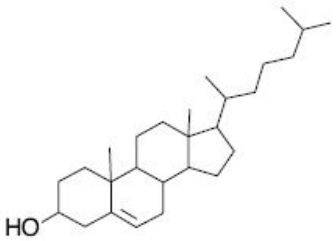
Фосфолипиды

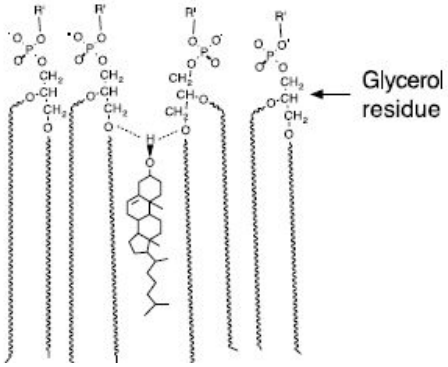


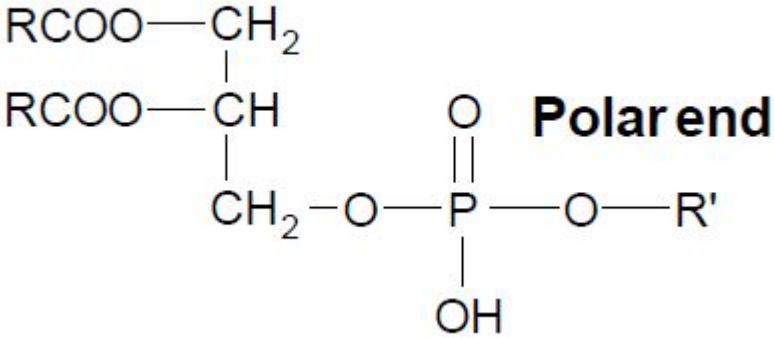
Сфинголипиды



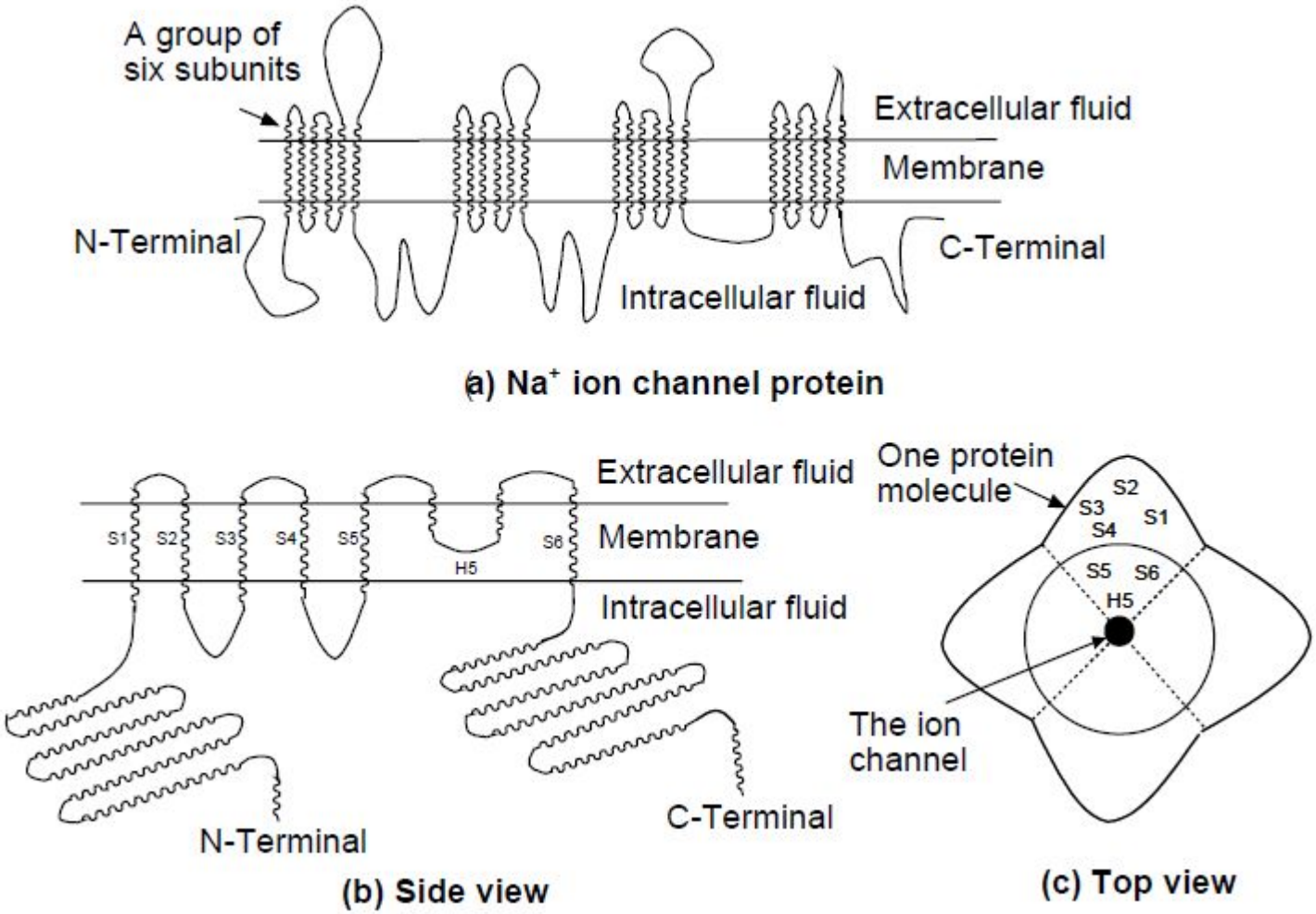
Холестерол



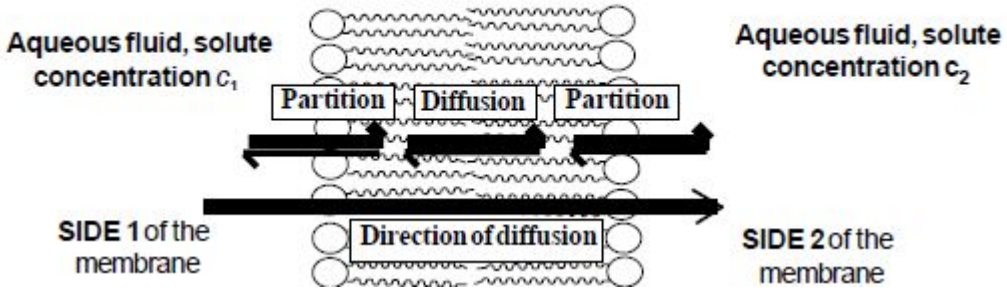


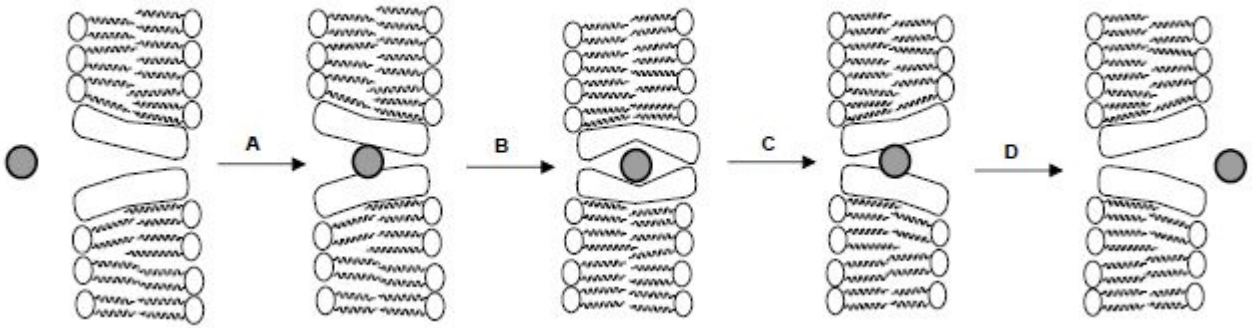


Мембрана и белки

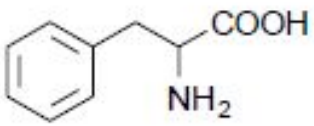


Активный и пассивный транспорт

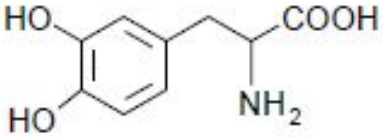




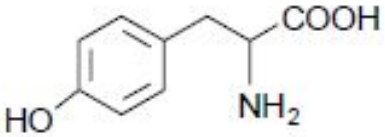
Активный транспорт



Phenylalanine



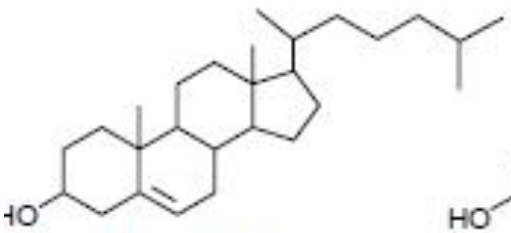
Levodopa



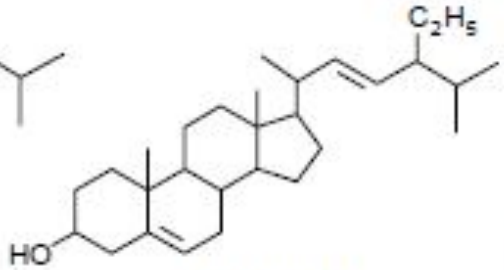
Tyrosine

Различие в мембранах

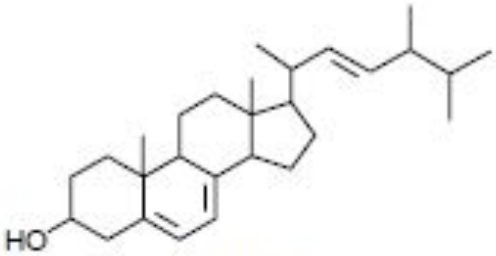
Compound	Animals	Bacteria	Fungi	Plants
Steroids	Cholesterol	Rare	Ergosterol (yeast and other fungi)	Stigmasterol Sitosterol Cytosterol
Phospholipids	PC, PE, DPG, SM	PC, PE, PI (cyanobacteria)		PC, PE, PI, DPG (chloroplasts)



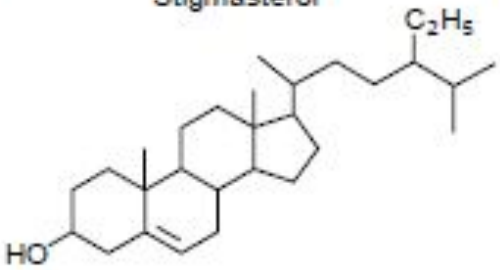
Cholesterol



Stigmasterol

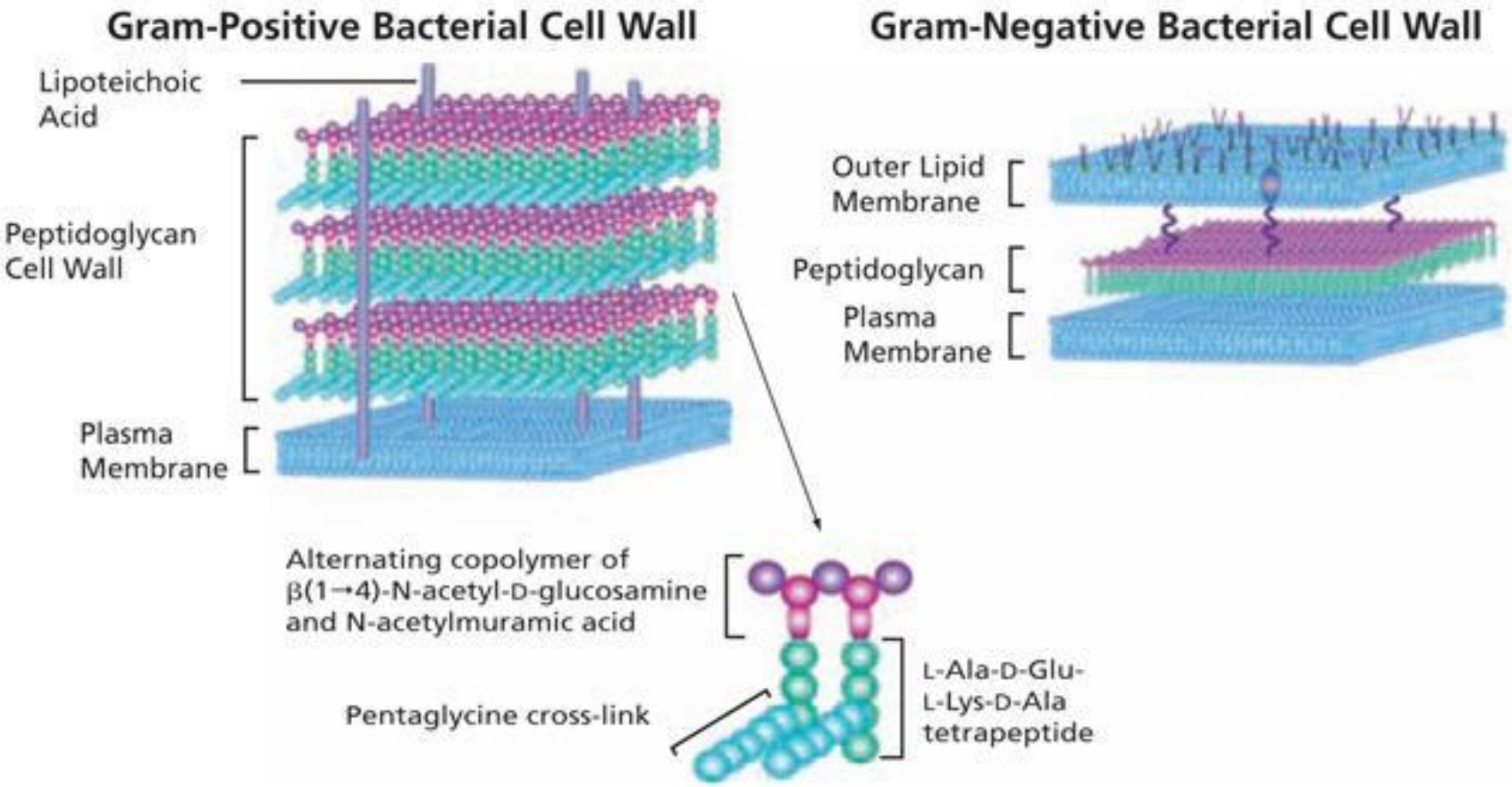


Ergosterol

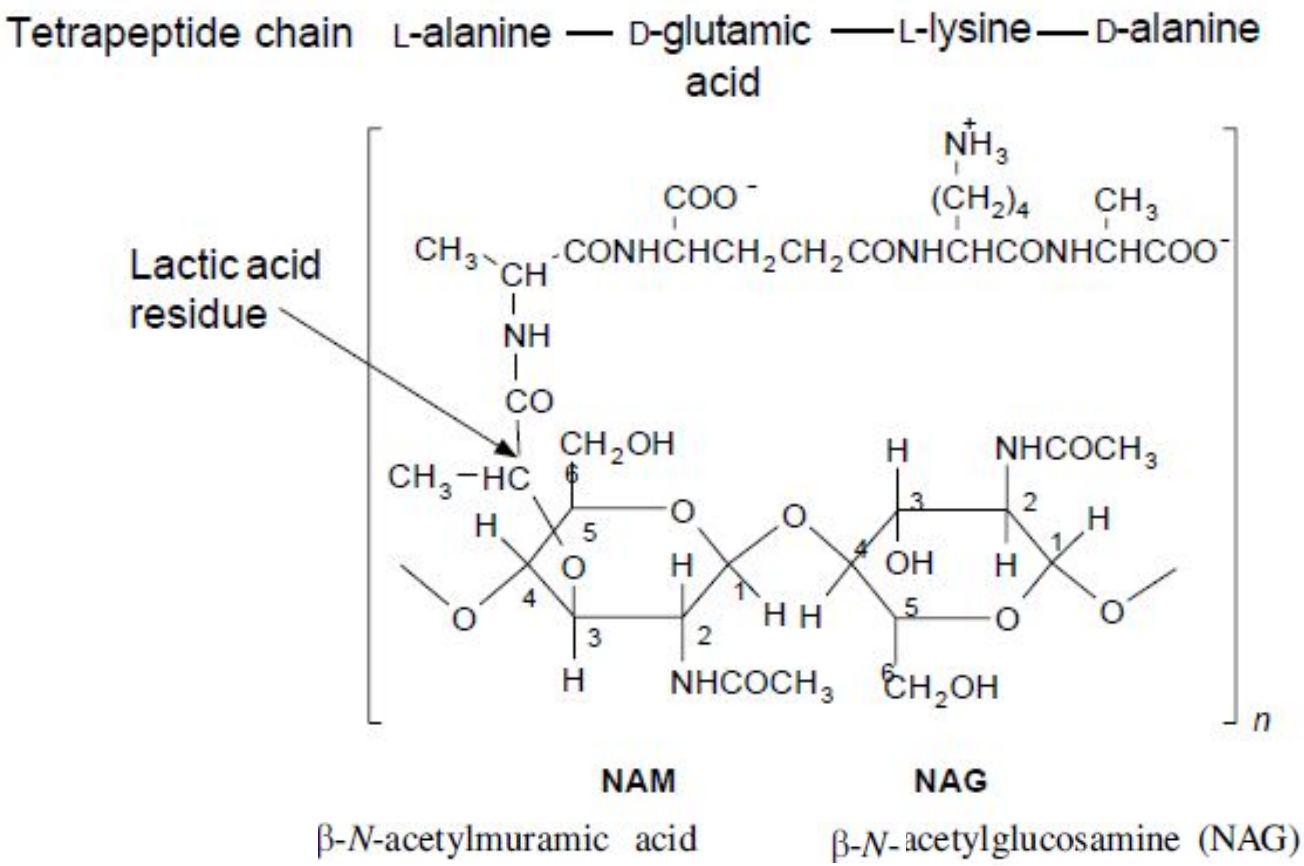


β-Sitosterol

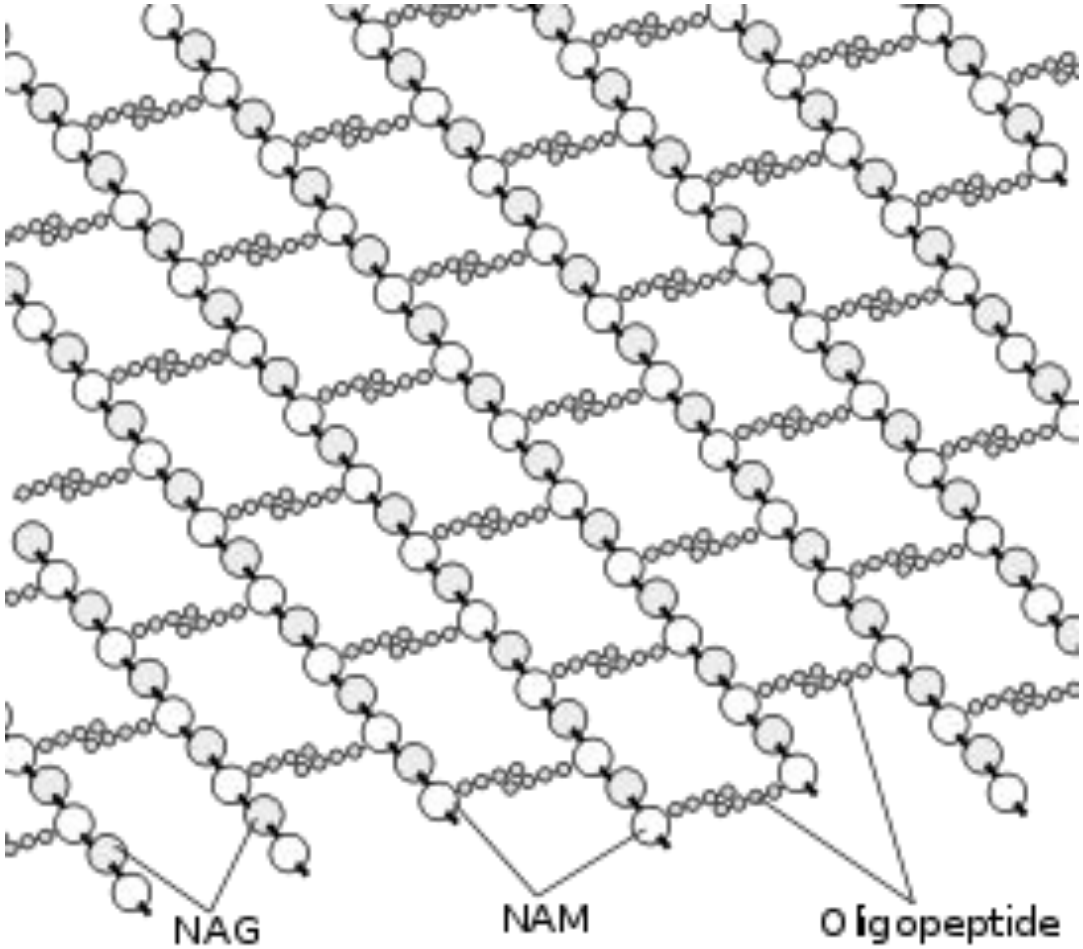
Строение клеточной стенки бактерий



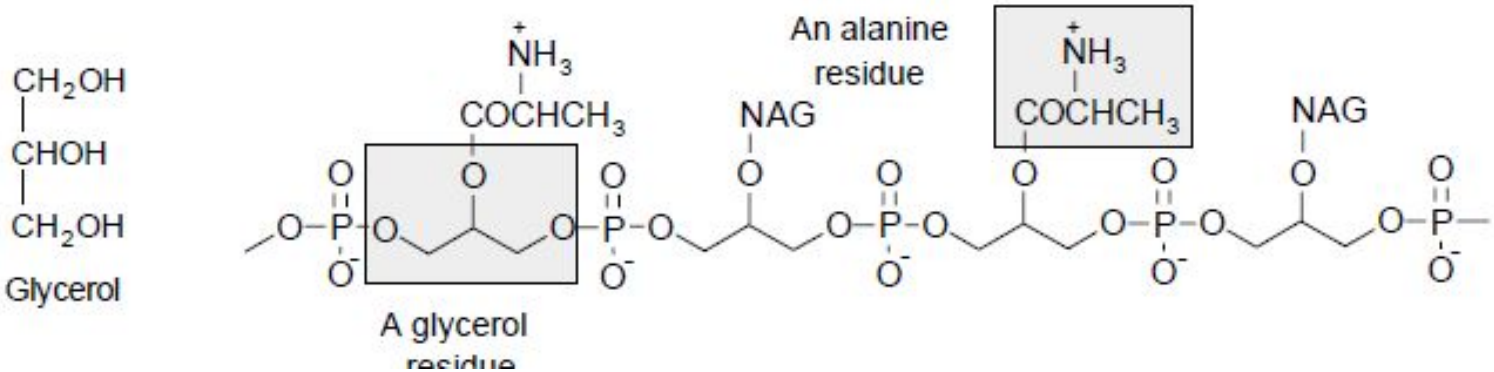
Пептидогликан



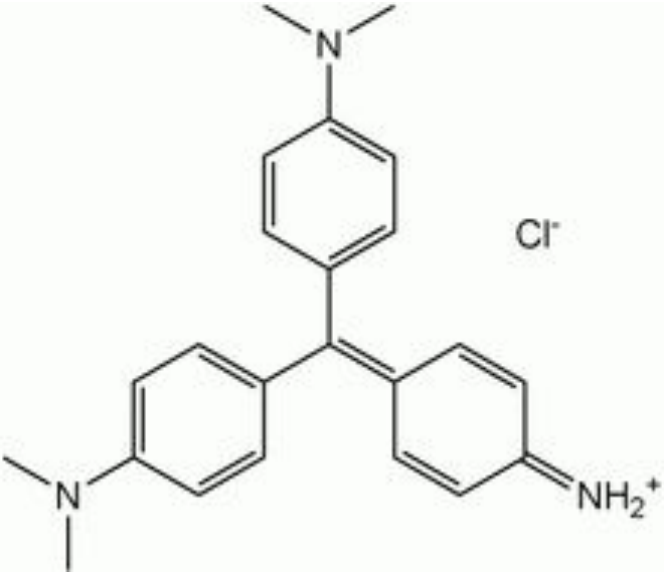
Клеточная стенка

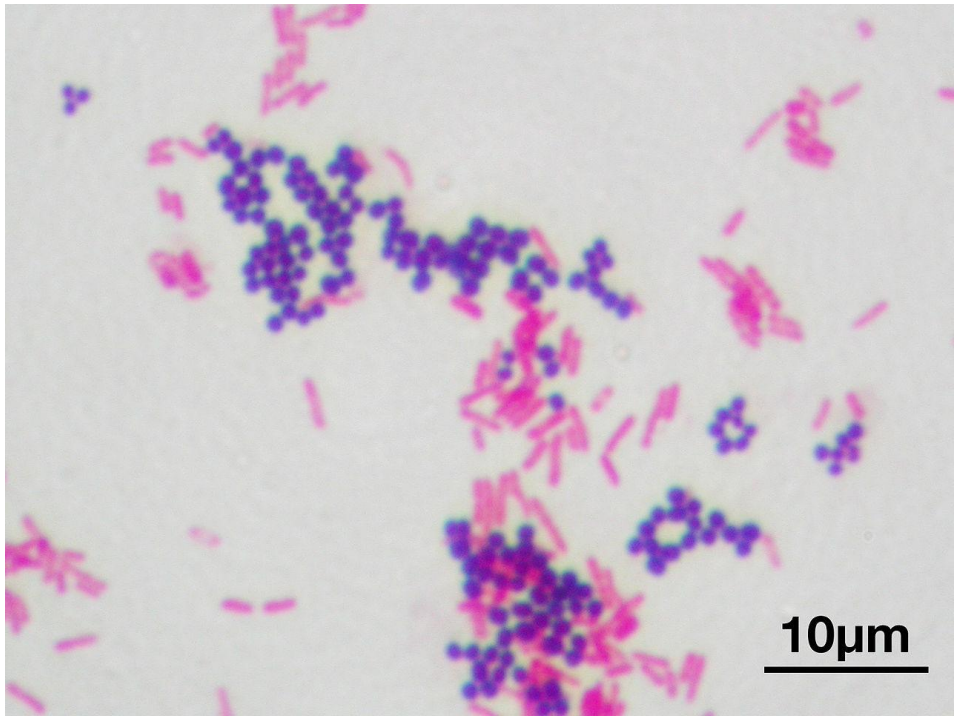


Тейхоевые кислоты



Окрашивание по Граму

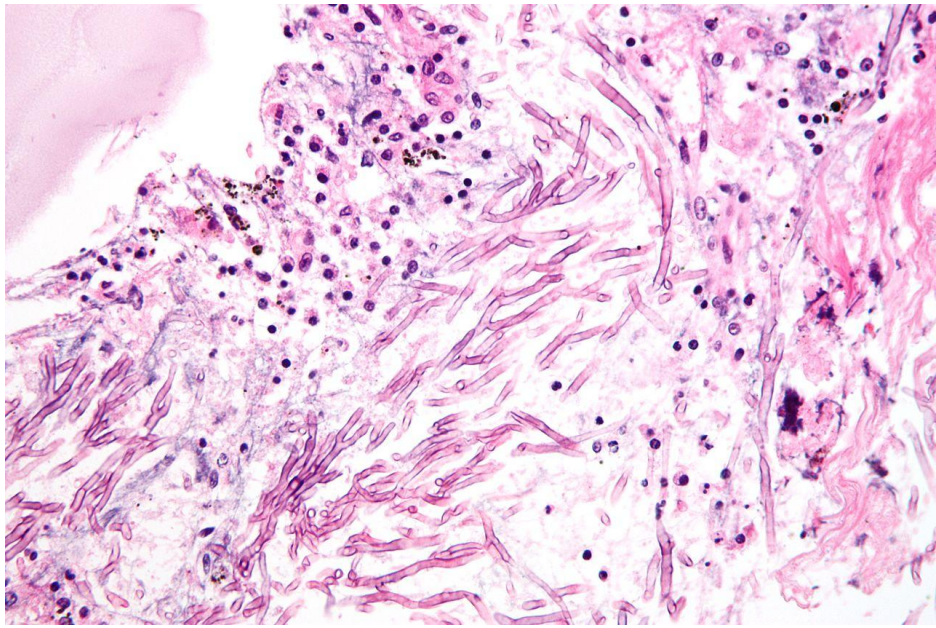




Классификация соединений, действующих на клеточные мембраны и стенку

- Ингибирование ферментов, отвечающих за синтез соединений необходимых для мембраны или стенки
- Ингибирование процессов образования клеточных стенок
- Образование каналов переноса веществ
- Изменение физико-химических свойств мембраны

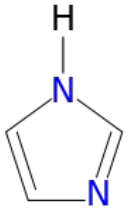
Противогрибковые соединения



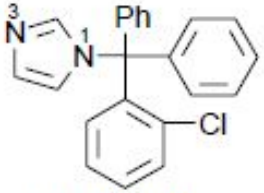
- Азолы
- Аллиламины
- Фенолы
- Другие

Противогрибковые соединения. Азолы

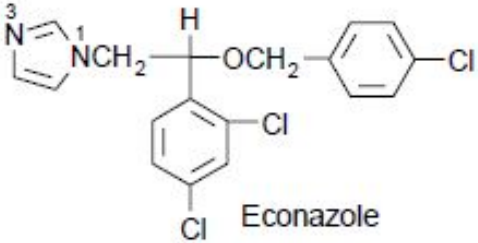
—эффективны против большинства грибов, инфицирующих кожу и слизистые оболочки



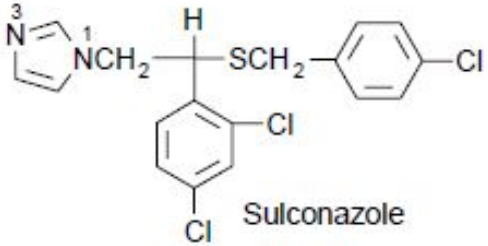
imidazole



Clotrimazole



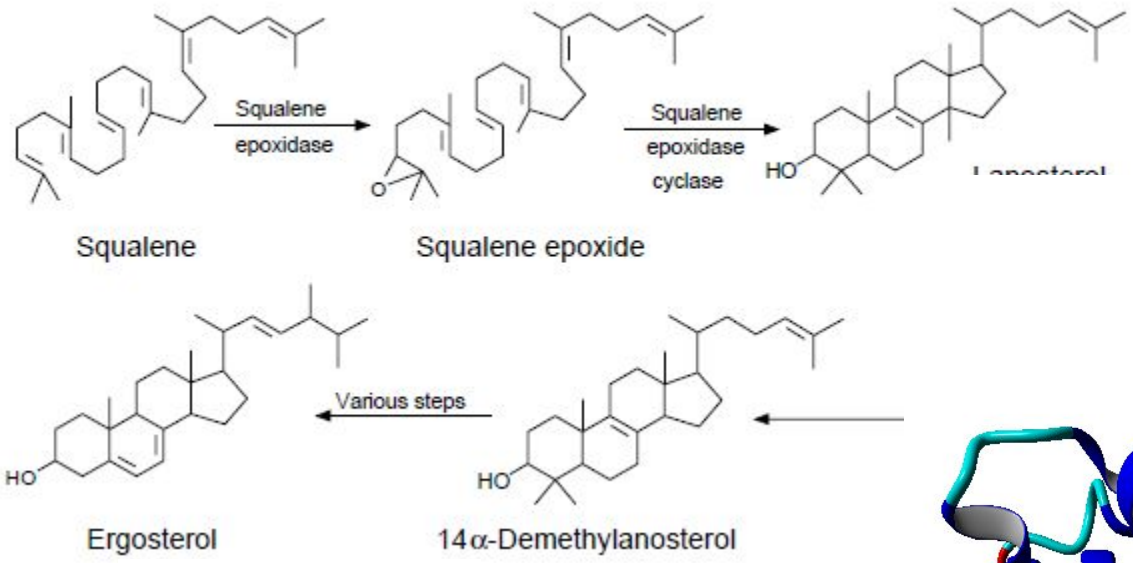
Econazole

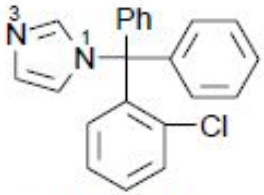


Sulconazole

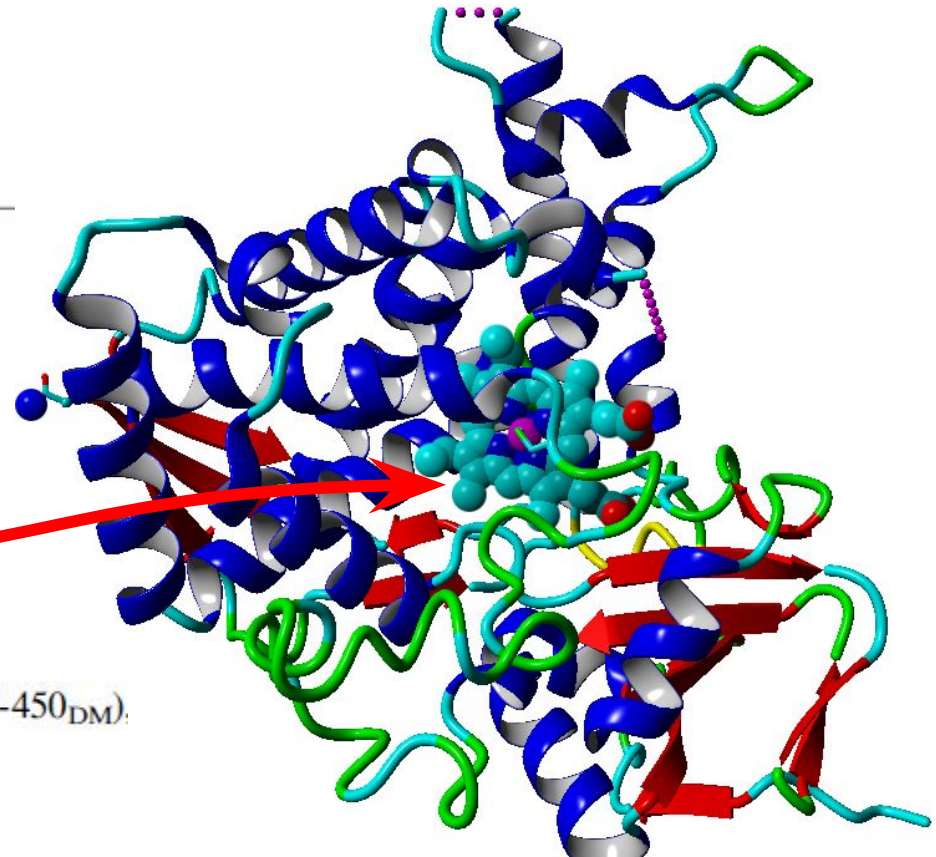
Местно, наносят тонким слоем на пораженные участки кожи и слизистых оболочек 2–4 раза в сутки. Курс лечения подбирают индивидуально, обычно — не менее 4 нед; по его завершении (исчезновение клинических проявлений) целесообразно продолжить применение препарата еще в течение 14 дней.

Азолы. Механизм действия





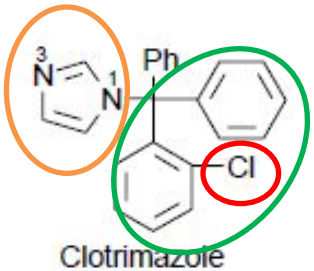
Clotrimazole

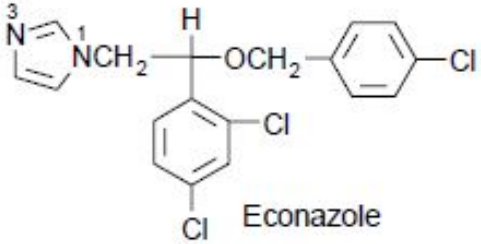


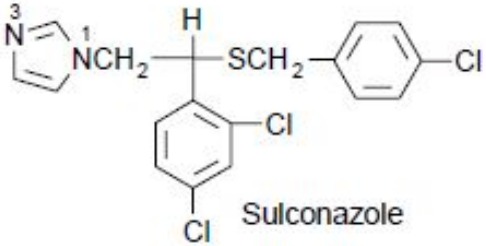
14α-sterol demethylase (P-450$_{DM}$).

Азолы. SAR

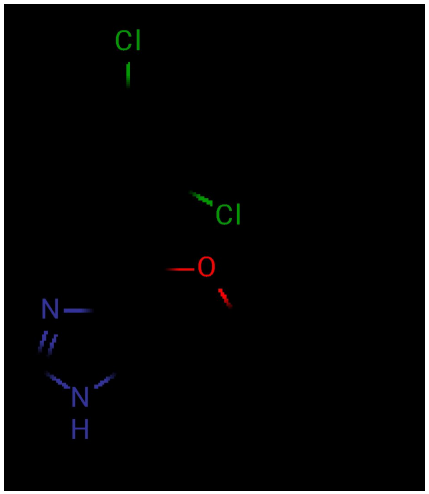
N-1 замещённые азолы или 1,2,4 триазолы. Заместители должны быть липофильными. Обычно они представляют собой 5 или 6 кольца, присоединённые через атом углерода с последующей эфирной связью, вторичным амином, тиоэфирной группой. Наиболее активные соединения содержат 2 или 3 ароматических кольца, моно- или полизамещённые в 2,4,6 положения (заместители хлор или фтор).







Азолы. SAR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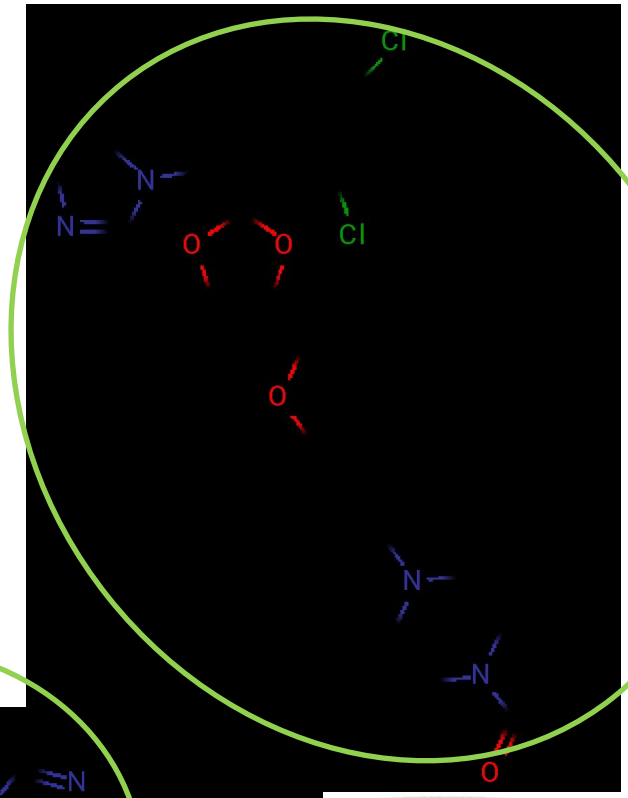
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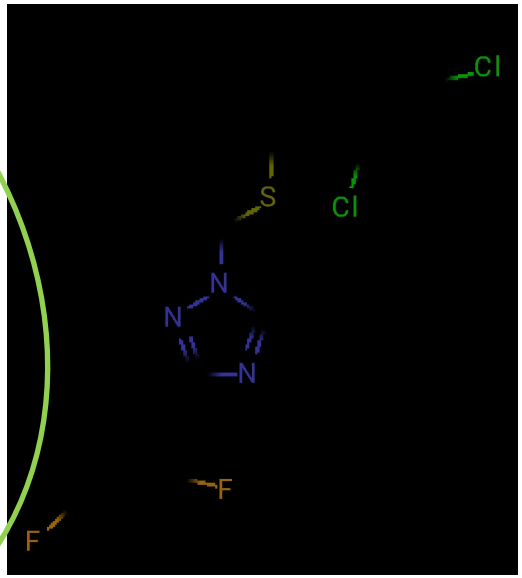
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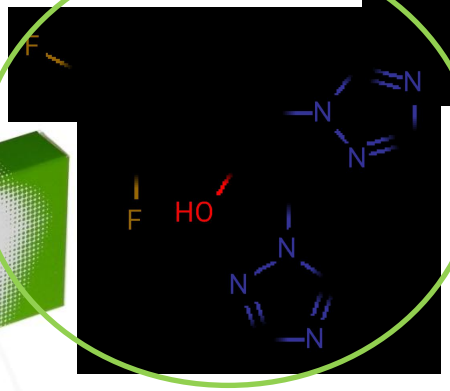
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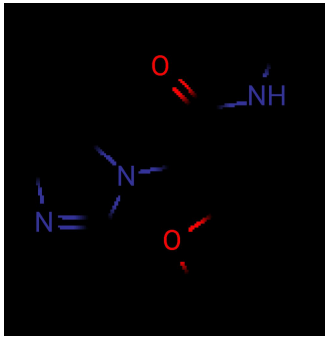
Флуконазол
150 мг
1 капсула
ВИЛОКОМ

NDC 51672-4026-1
Ketoconazole
Tablets USP
200 mg
Each tablet contains:
Ketoconazole 200 mg
Rx only
100 Tablets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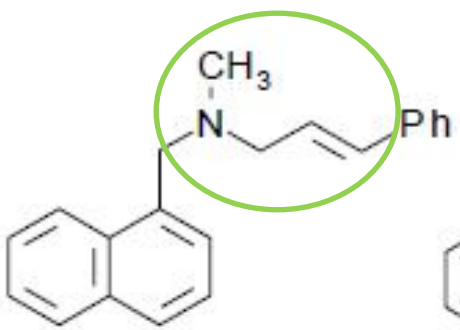
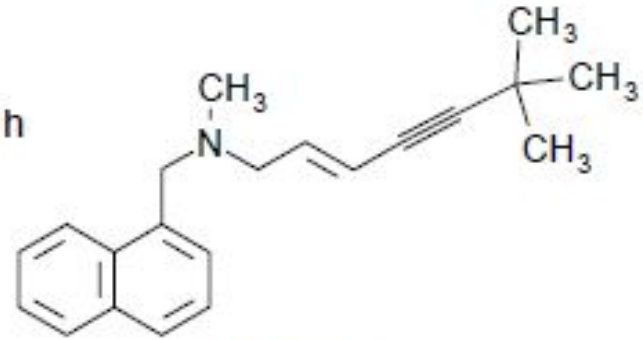
Противогрибковые соединения. Аллиламины

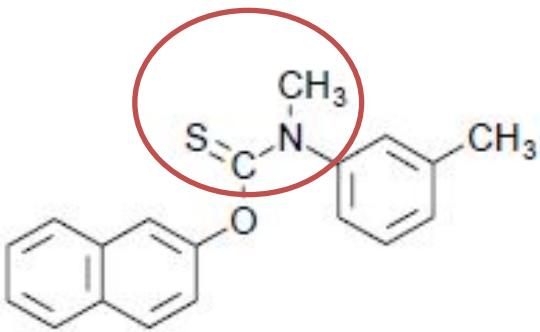
—ингибируют сквален монооксидазу



Naftifine



Terbinafine

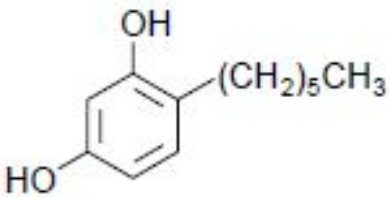


Tolnaftate

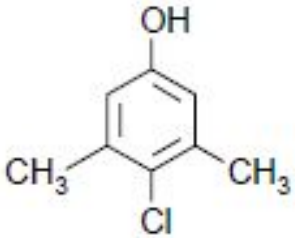
Грибковые поражения кожи, ногтей и волос, кандидоз кожи и слизистых оболочек.

Противогрибковые соединения. Фенолы

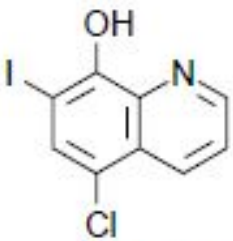
— разрушают отдельные участки мембраны



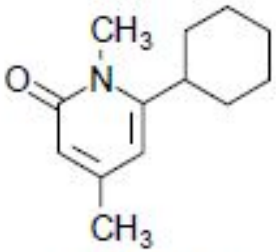
Hexylresorcinol



Chloroxylenol

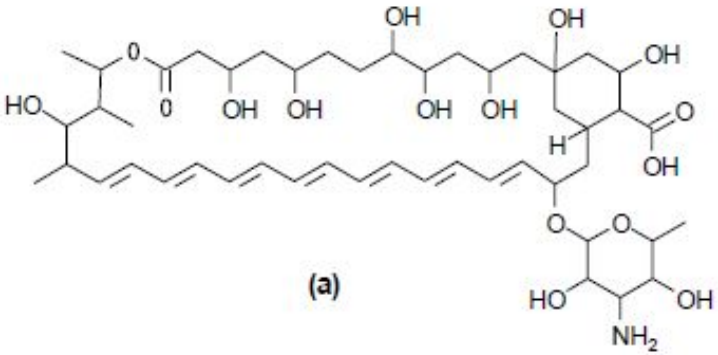


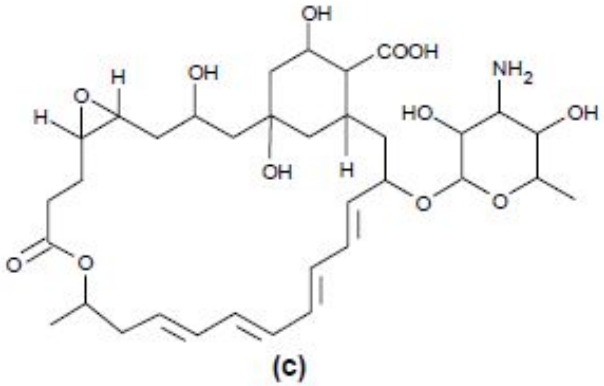
Clioquinol



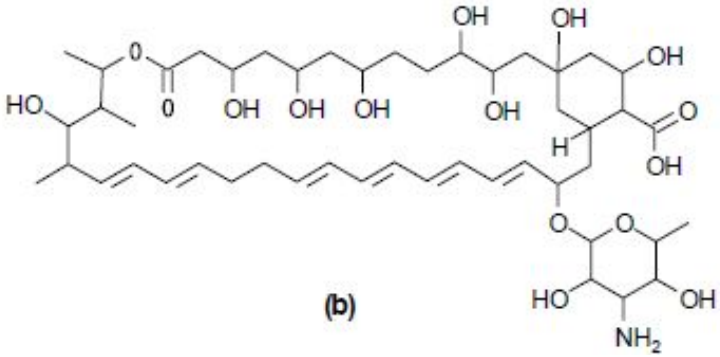
Ciclopirox

Антибиотики с противогрибковым действием

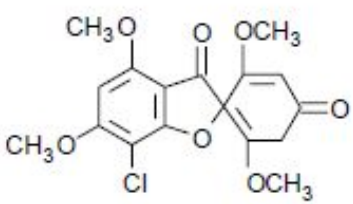




Amphopterin B,



Natamycin

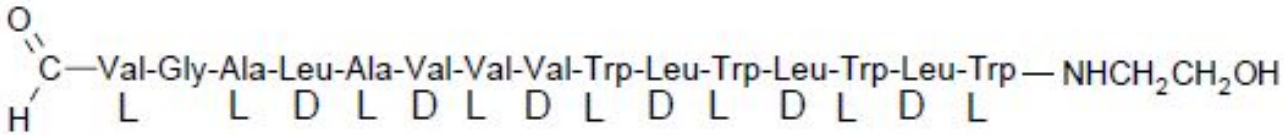


Nystatin,

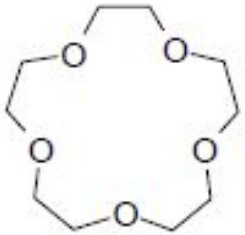
Griseofulvin

Антибиотик, продуцируемый плесневым грибом *Penicillium nigricans (griseofulvum). Действует на микротубулярные белки гриба.*

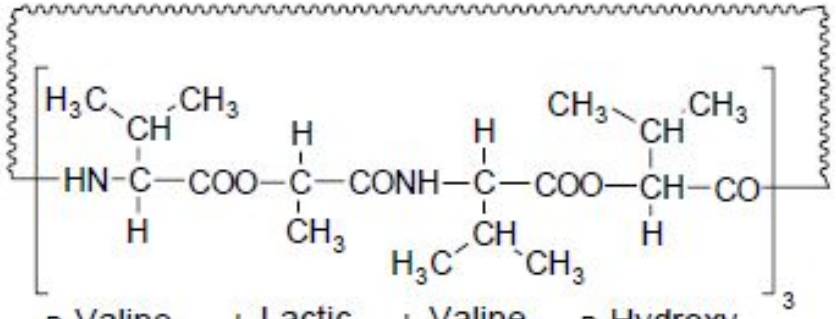
Антибиотики. Ионофоры



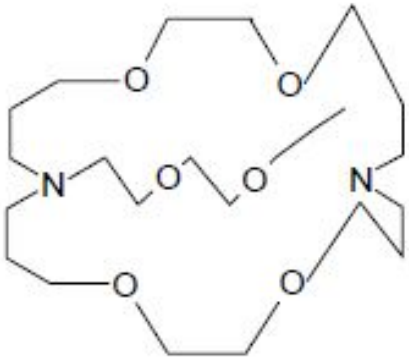
Gramicidin A



15-Crown-5

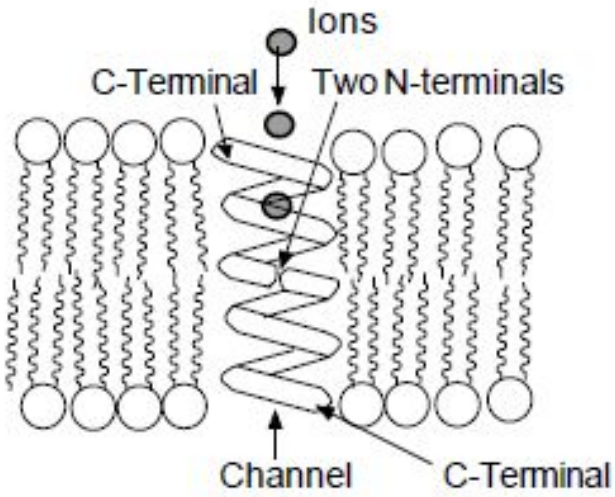


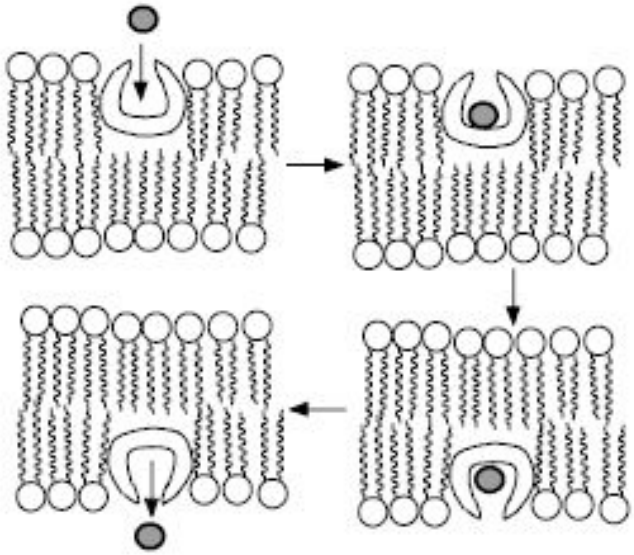
Valinomycin



A cryptate

Ионофоры. Механизм действия

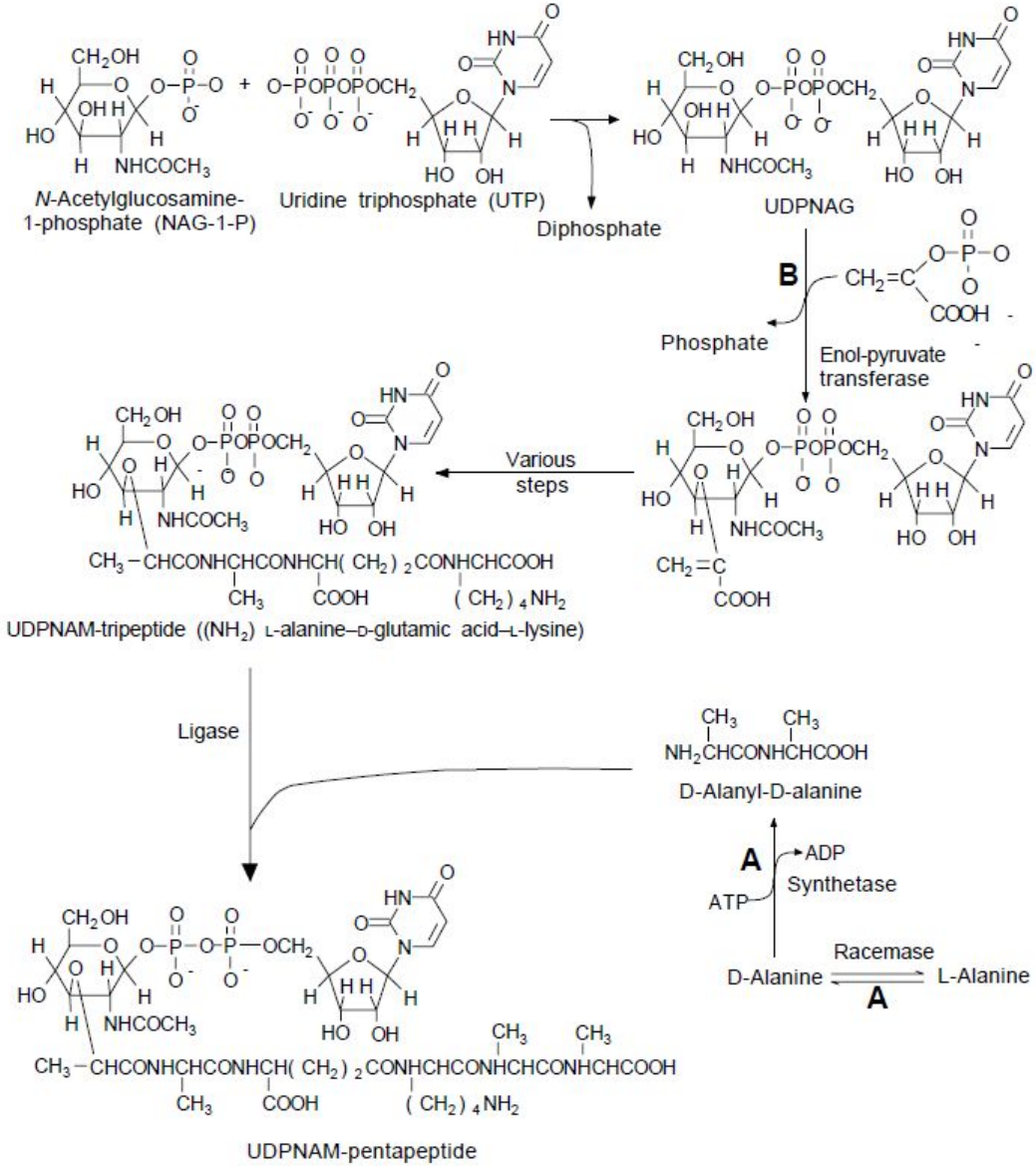




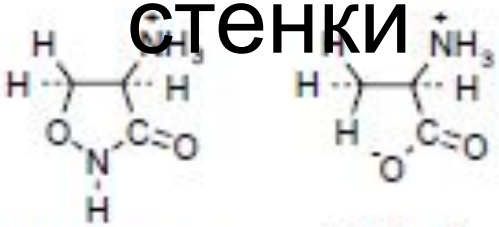
Ингибиторы синтеза клеточной стенки

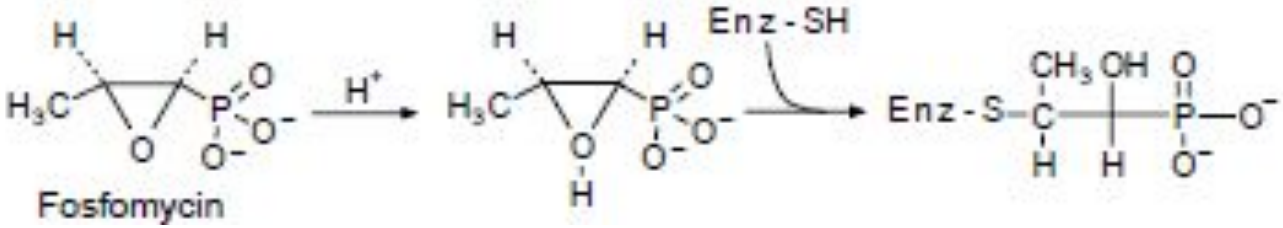
- Ингибиторы синтеза прекурсоров исходных материалов для клеточной стенки
- Ингибиторы образования пептидогликановых цепей
- Ингибиторы сшивания пептидогликановых цепей

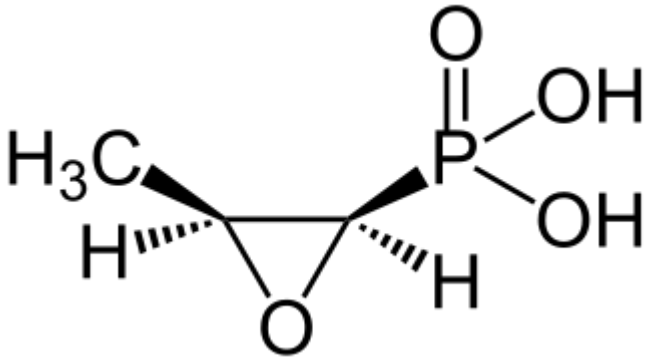
Ингибирование синтеза прекурсоров исходных материалов клеточной стенки



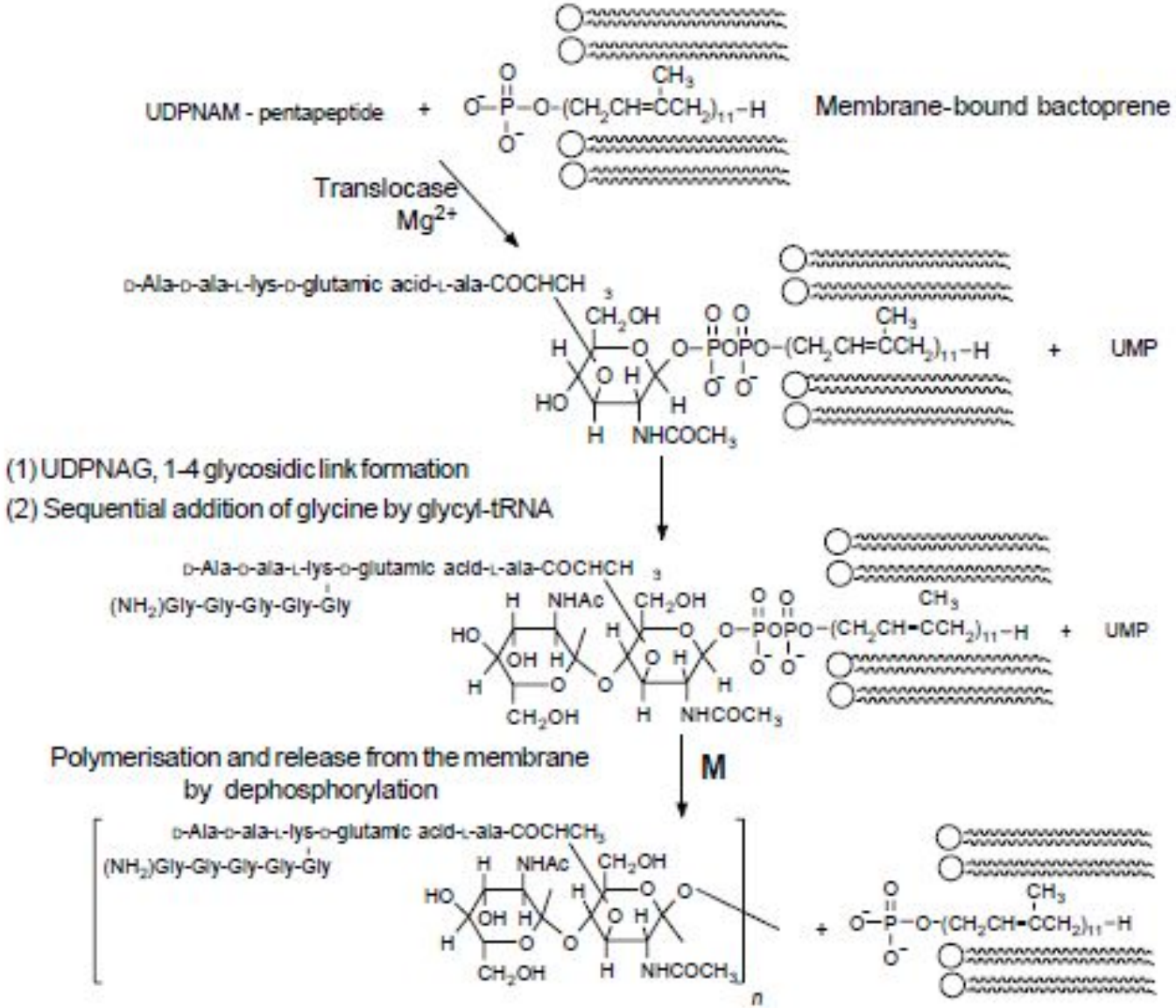
Ингибирование синтеза прекурсоров исходных материалов клеточной стенки



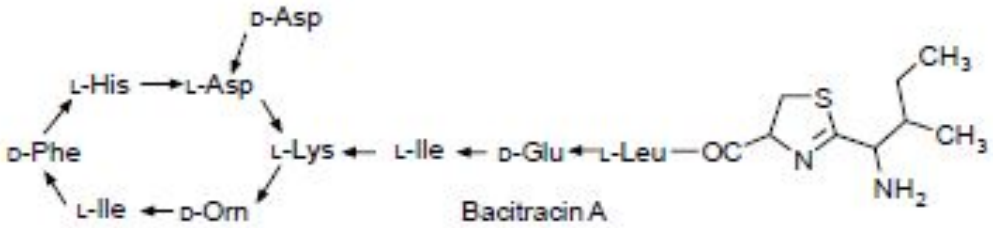


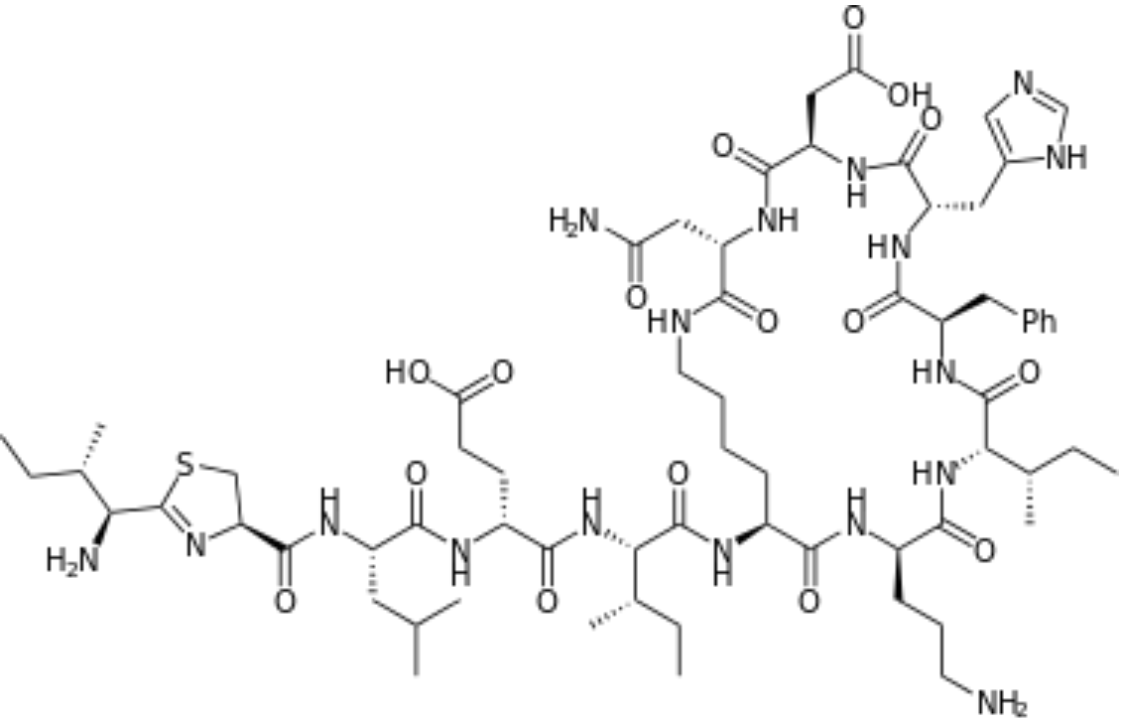


Ингибирование синтеза клеточной стенки



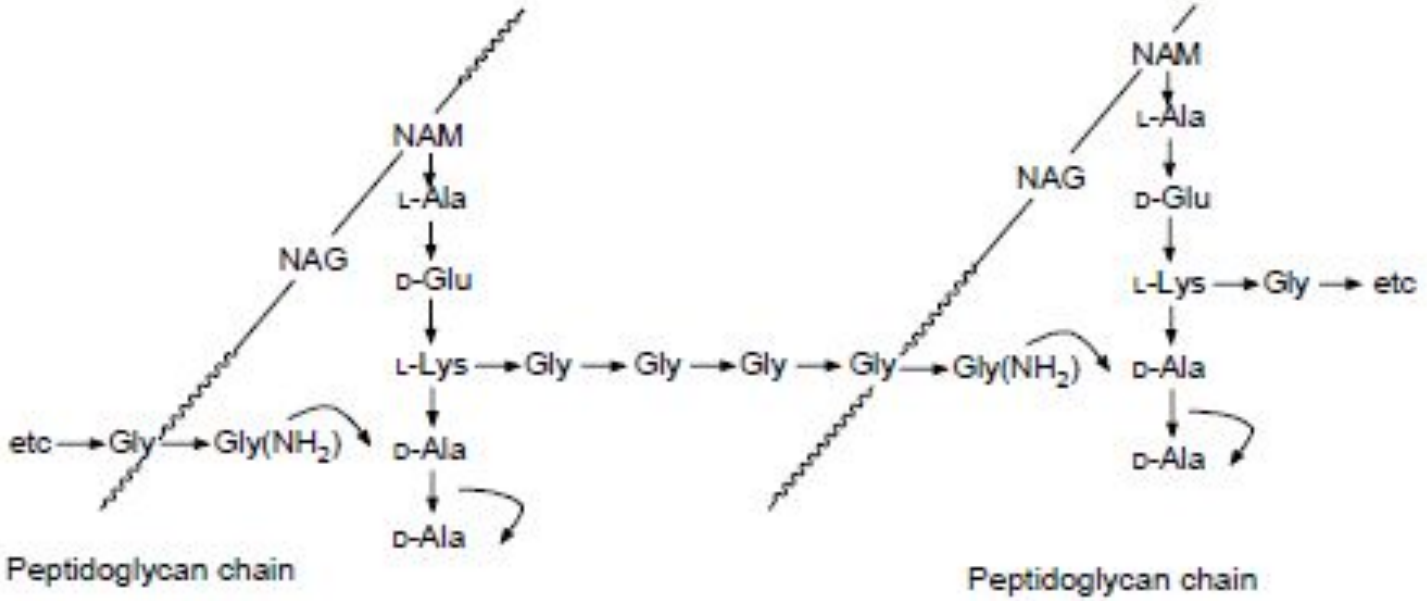
Бацитрацин


D-Asp
L-His
L-Asp
D-Phe
L-Lys
L-Ile
D-Glu
L-Leu
OC
L-Ile
D-Orn
Bacitracin A

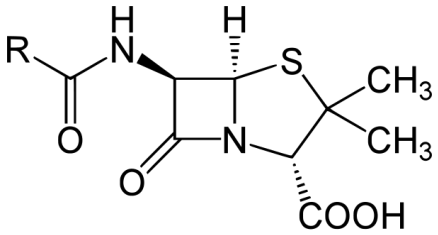


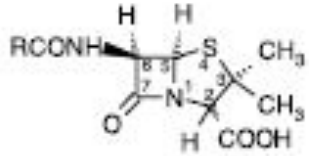
RITE AID
Bacitracin
OINTMENT, USP
First Aid Antibiotic
To help prevent infection in minor cuts, scrapes, and burns
RITE AID
Bacitracin
FIRST AID ANTIBIOTIC OINTMENT
OINTMENT, USP
NET WT. 1 OZ (28 g)

Ингибиторы «сшивки» стенки

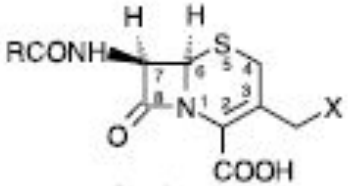


Ингибиторы «сшивки» стенки

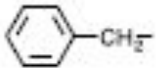
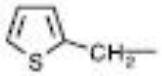
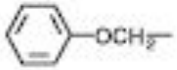
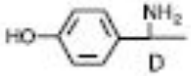
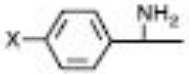
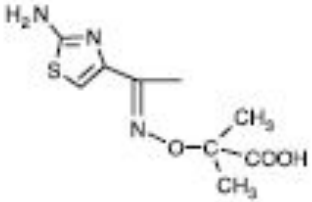
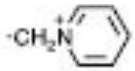
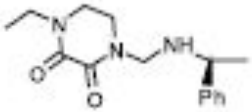
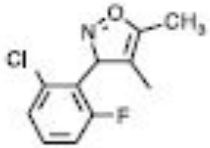
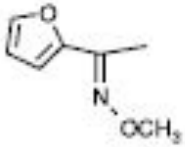
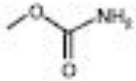




Penicillins

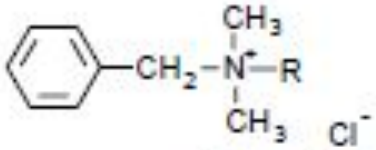


Cephalosporins

Penicillin	R-	Cephalosporins	R-	X-
Benzylpenicillin (Penicillin G)		Cephalothin		$-OCOCH_3$
Phenoxymethylpenicillin (Penicillin V)		Cefadroxil		$-H$
Ampicillin (X = H) Amoxicillin (X = OH)		Ceftazidime		
Piperacillin				
Flucloxacillin		Cefuroxime		

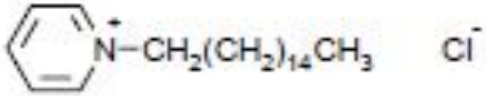
ПАВы

Cationic surfactants



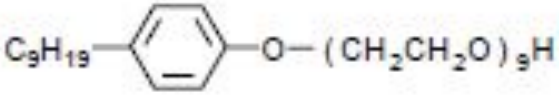
Where R is a mixture of C_8H_{17} to $C_{18}H_{37}$ residues

Benzalkonium chloride

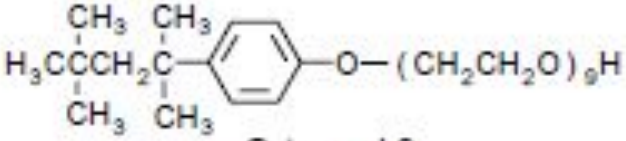


Cetylpyridinium chloride

Non-ionic surfactants



Nonoxynol-9



Octoxynol-9