

# Фармацевтична Химия



## Тема 8

### Психостимуланти & Ноотропни лекарства

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## ПСИХОСТИМУЛАНТИ И НООТРОПНИ ЛЕКАРСТВА

**ПСИХОСТИМУЛАНТИ:**

подобряват процесите на възбуда; ускоряват образуването на условни рефлекс; възстановяват потиснати рефлексии.

**Допинг амини (адреномиметици с психостимулиращо действие):**

стимулират централните и периферни адренергични и допаминергични неврони и облекчават отделянето на норадреналин и допамин.

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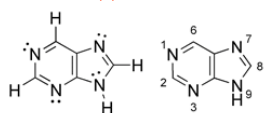
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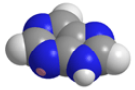
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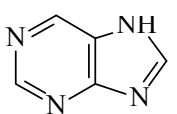
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**ПУРИН И ПРОИЗВОДНИ**

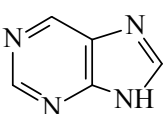






7H-purine

$\rightleftharpoons$



9H-purine

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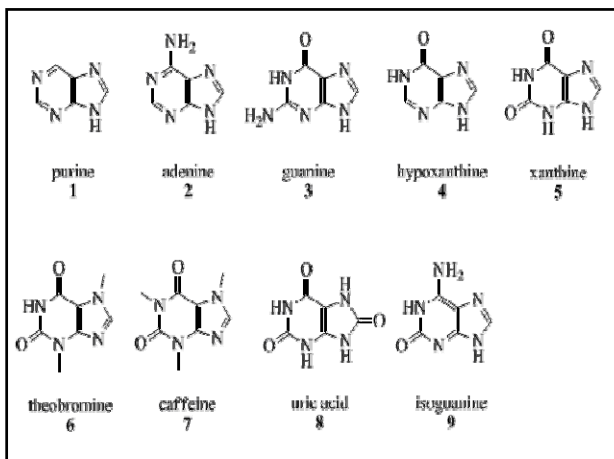
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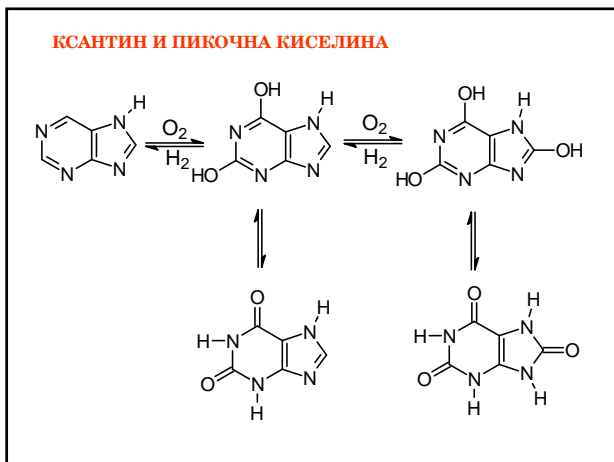
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**ПУРИНИ и КСАНТИНИ**

- Психостимуланти
- Бронходилататори
- Вазодилатори
- Антинеопластични
- Противовирусни
- Диуретици

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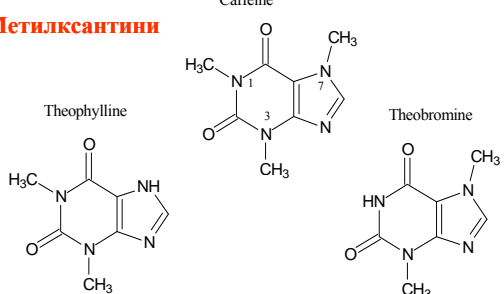
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## ПСИХОСТИМУЛАНТИ

### Метилксантини



**1,3,7-trimethyl-1H-purine-2,6(3H,7H)-dione**  
**1,3,7-trimethylxanthine, trimethylxanthine, theine, mateine, guaranine, methyltheobromine**

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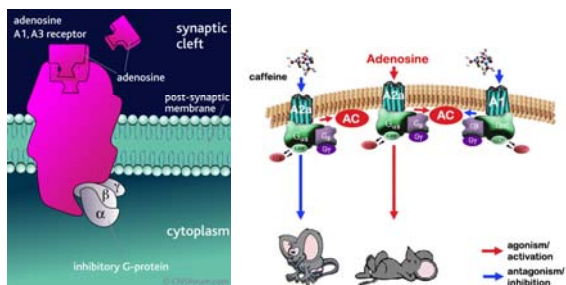
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**Механизъм на действие:** кофеинът е неселективен антагонист на  $A_1$  и  $A_2$  аденозиновите рецептори. Засилва възбудните процеси, а по механизма на положителната индукция подобрява процесите на задържане.




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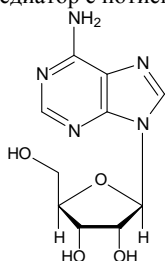
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Кофеинът е неселективен антагонист на  $A_1$  и  $A_2$  аденозиновите рецептори и така се **предотвратява** ефекта на аденозина, медиатор с потискащо действие.

### Adenosine

нуклеозид



Кръвното налягане се повишава от **кофеина**, понижава се от **теофилина** и не се повлиява от **теобромна**.

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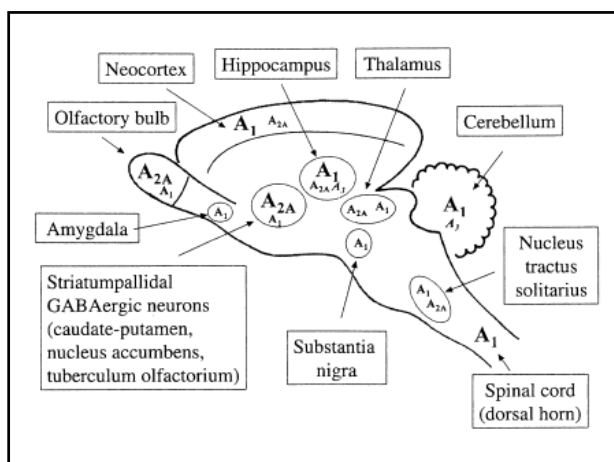
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Конвулсивното действие при токсични концентрации може да се обясни с достигане до почти пълно инхибиране на мозъчната фосфодиестераза;

Кофеинът е аналептик на вазомоторния и дихателния център, като този ефект е най-подчертан при теофилина и неговите производни, което обуславя и тяхното широко приложение за лечение на бронхообструктивни заболявания;

Механизмът на диуретичното действие на кофеина е комплексен. Подобрявайки бъбречната хемодинамика чрез своите ефекти върху сърцето и бъбречните съдове, той увеличава гломерулната филтрация. Наред с това той намалява реабсорбцията на  $\text{Na}^+$  и  $\text{Cl}^-$  в проксималните бъбречни каналчета. Също така той намалява хидрофилността на тъканите, а с това увеличава плазменния обем на кръвта. Това от своя страна по рефлекторен път чрез стимулация на т. нар. обемни рецептори води до инхибиране на секрецията на антидиуретичния хормон и респективно до увеличаване на диурезата.

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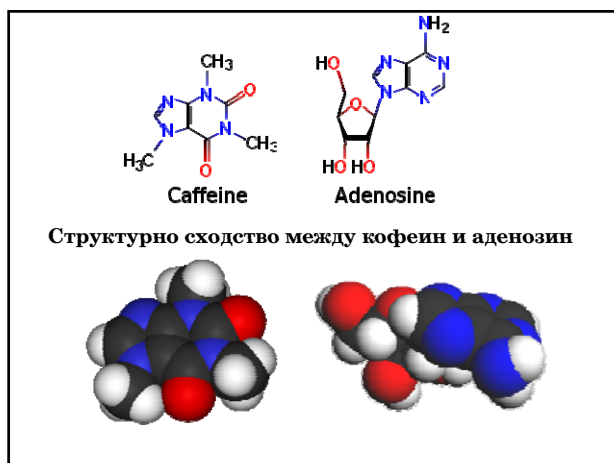
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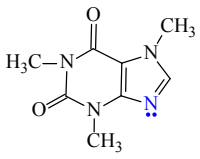
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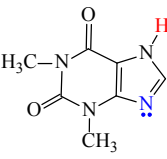
*Ph Eur*

**Caffeine**



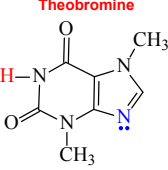
**Caffeine Hydrate**  
Central nervous stimulant  
1,3,7-trimethyl-3,7-dihydro-1H-purine-2,6-dione  
Aspirin and Caffeine Tablets

**Theophylline**



Xanthine bronchodilator  
1,3-dimethyl-3,7-dihydro-1H-purine-2,6-dione  
Aminophylline Injection  
Prolonged-release Theophylline Tablets

**Theobromine**



3,7-dimethyl-3,7-dihydro-1H-purine-2,6-dione

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**Връзка структура-действие:** Действието на метилксантините зависи от броя и местоположението на метиловите групи. Изведени са следните зависимости:

1. Наличие на  $CH_3$ -група на 1-во място - действие върху ЦНС
2. Наличие на  $CH_3$ -група на 3-во място - диуретично действие
3. Наличие на  $CH_3$ -група на 7-во място - действие върху сърдечния мускул

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**Caffeine - психостимулант**

Theophylline – бронходилататор  
Theobromine – диуретик

**CAFFEINE PER AVERAGE CUP OR BAR (MG):**

ground coffee 90; instant coffee 60;  
decaffeinated coffee 3; tea 40; cola 40;  
chocolate bar 40.

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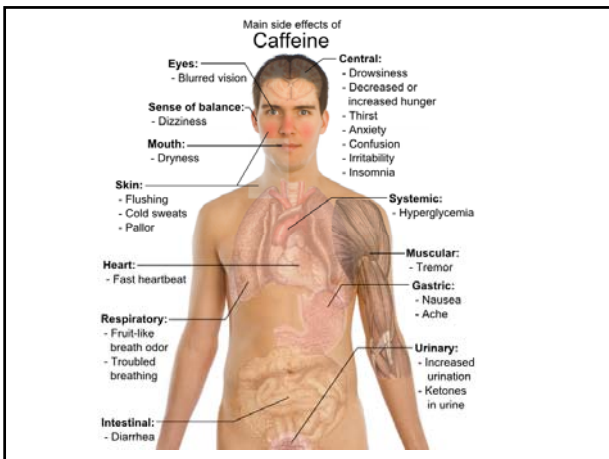
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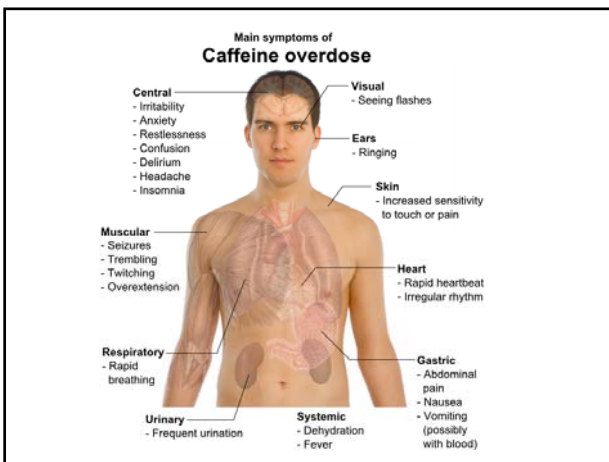
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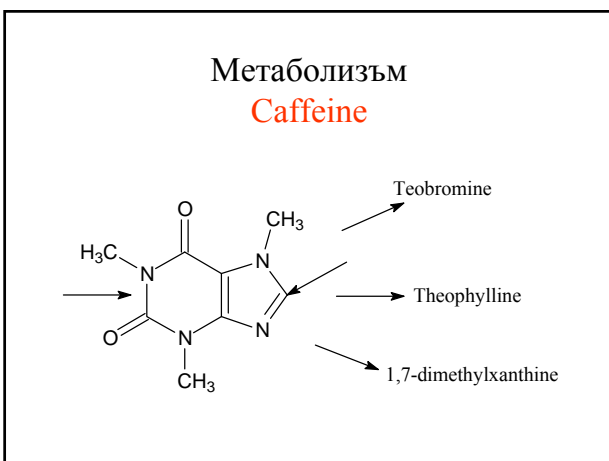
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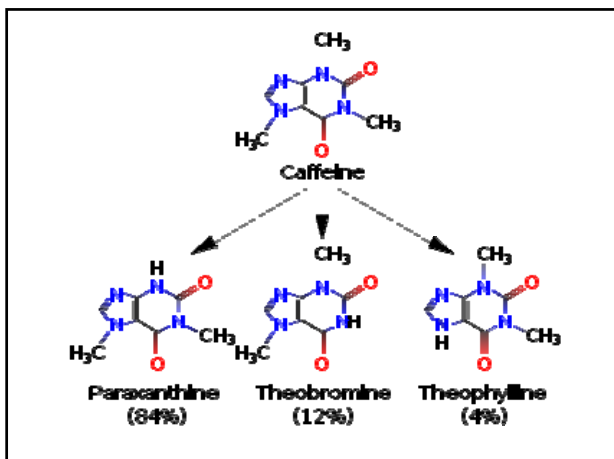
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**Киселинно – основни свойства на метилксантините**

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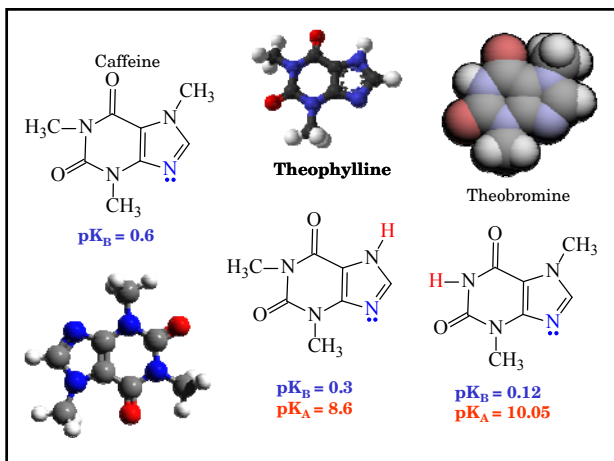
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Разтворимост и температура на топене на някои пурины и ксантини

Разтворимост във вода m.p. °C at room temp.

|              |         |                       |
|--------------|---------|-----------------------|
| Purine       | 1:2     | 216                   |
| Xanthine     | 1:15000 | разлагане без стапяне |
| Caffeine     | 1:60    | сублимира над 178     |
| Theophylline | 1:120   | 270-274               |
| Theobromine  | 1:3600  | над 350               |

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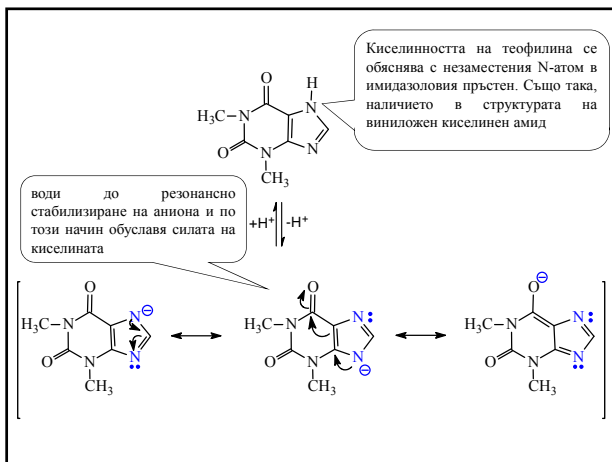
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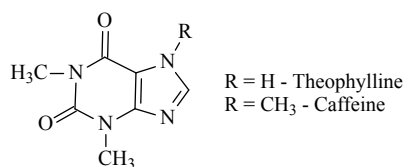
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Кофеинът и теофилинът в силно алкални водни разтвори се разпадат до кофеидин и теофилидин, тъй като активността на CO-групата на 2-ро място не е намалена, защото те имат заместители при N<sup>1</sup> и N<sup>2</sup>. Процесът зависи от температурата на реакционната среда и протича по схемата:

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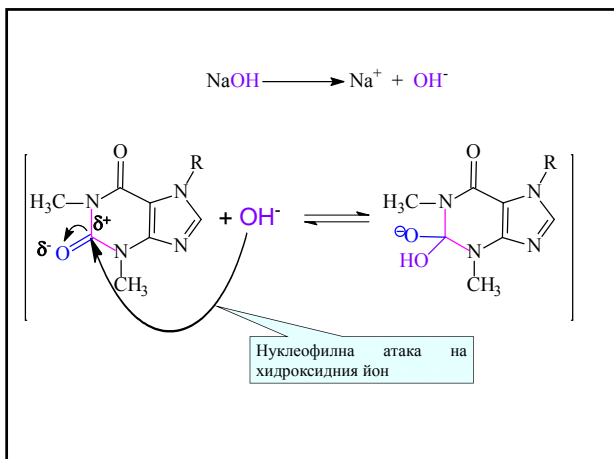
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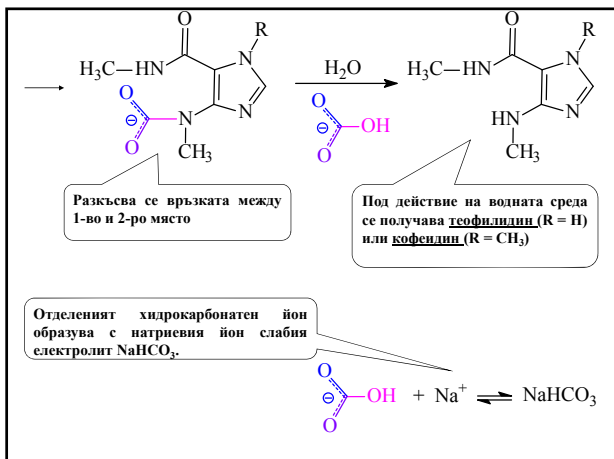
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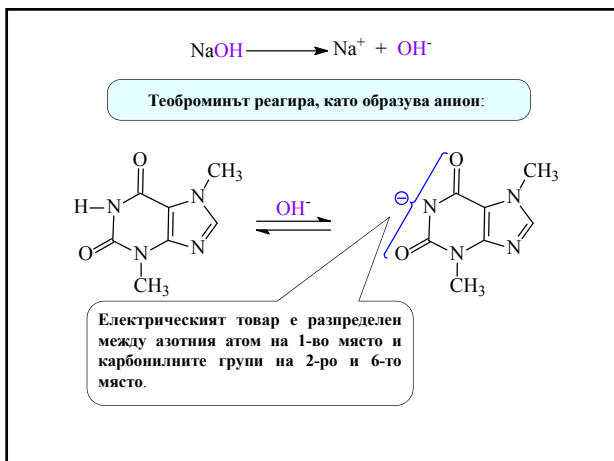
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## Получаване на метилксантини

### МЕТОД НА ТРАУБЕ

Wilhelm Traube (1866, Ratibor – 1942, Berlin)  
професор по химия в Берлинския Университет

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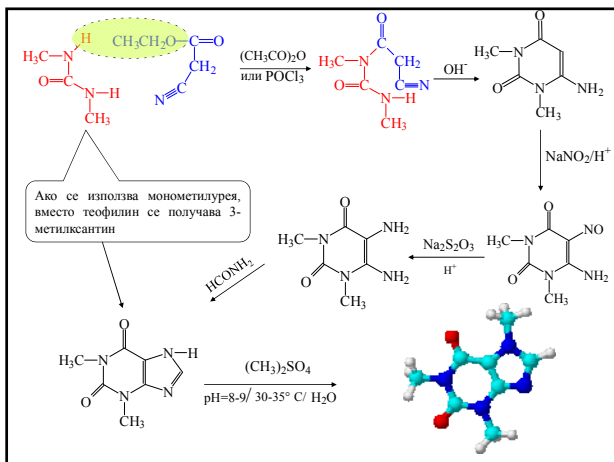
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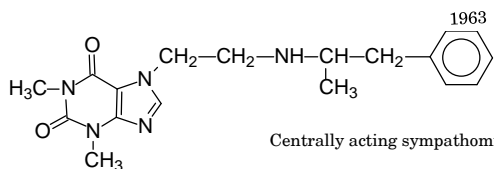
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### Fenethylline (Biocapton, Captagon)



3,7-dihydro-1,3-dimethyl-7-[2-[(1-methyl-2-phenylethyl)amino]ethyl]-1H-purine-2,6-dione

(RS)-1,3-dimethyl-7-[2-(1-phenylpropan-2-ylamino)ethyl]purine-2,6-dione

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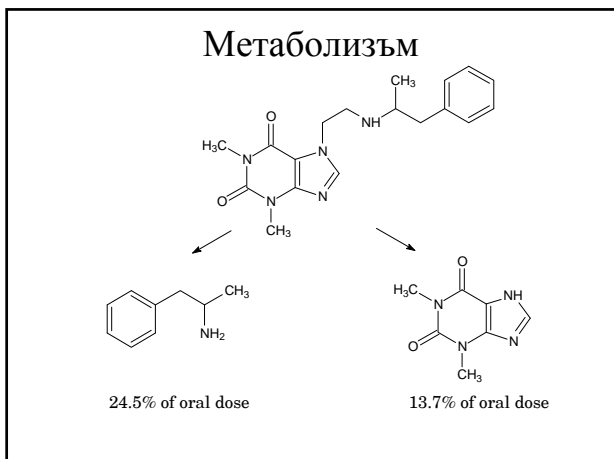
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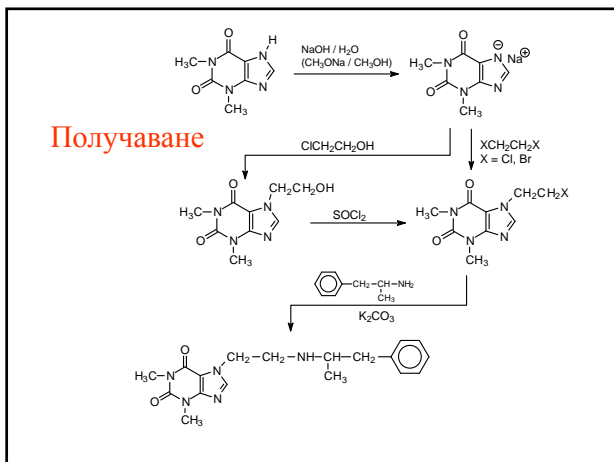
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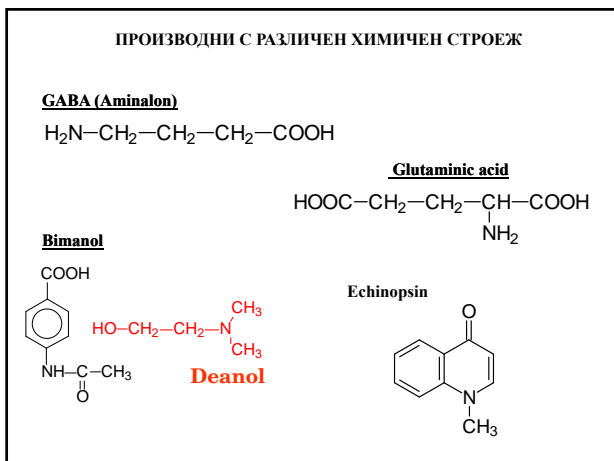
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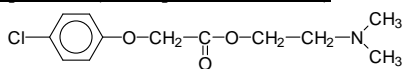
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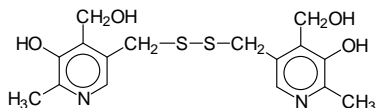
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**Meclophenoxat (Centrophenoxin, Lucidril)**

*N,N*-диметиламиноэтил 4-хлорофеноксиацетат

**Pyritinol (Enerbol, Encephabol)**

бис(3-гидрокси-4-гидроксиметил-2-метилпиридил-5)-метилдисульфид

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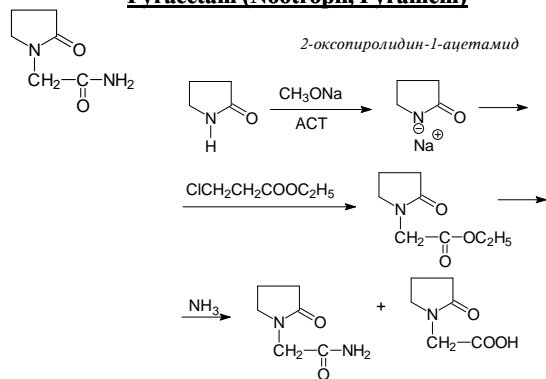
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**Pyracetam (Nootropil, Pyramem)**


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