

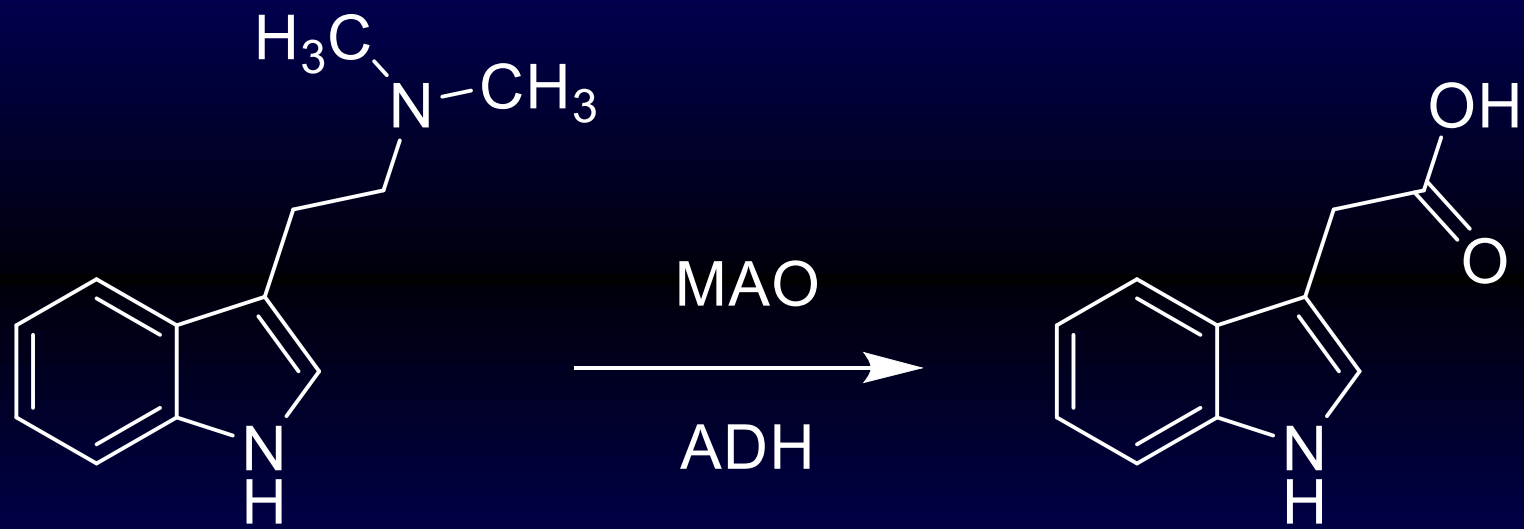
Psychedelic Therapeutics: Clinical Needs, Research Leads

Nicholas V. Cozzi, Ph.D.

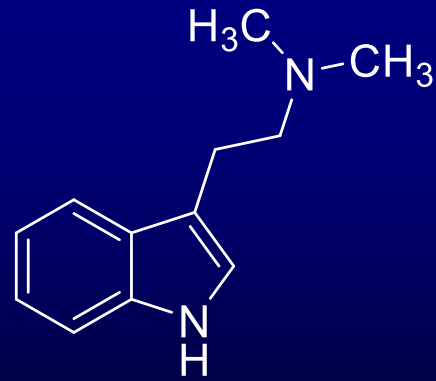


Room for improvement

- Off-target activity
- Pharmacokinetics
 - Too short (< 60 min) or too long (> 4 hr)
 - Want orally-active compounds
 - Avoid problematic metabolites
- Adverse effects
 - Sympathomimetic effects, serotonin syndrome
 - Gastrointestinal effects
 - Drug interactions
 - Post-session depression



Metabolism of DMT by monoamine oxidase and aldehyde dehydrogenase



N,N-Dimethyltryptamine (DMT)



N,N-Diallyltryptamine (DALT)



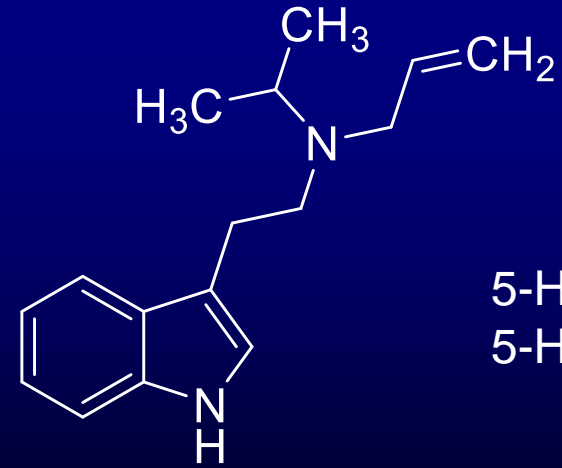
5-MeO-*N,N*-Diallyltryptamine (5-MeO-DALT)

Chemical structures of DMT and DALT compounds



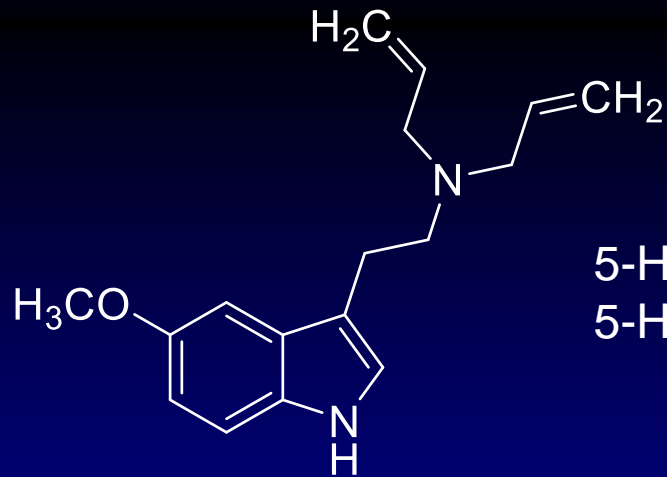
5-HT_{2A} = 708 nM
5-HT_{2B} = 62 nM

DALT



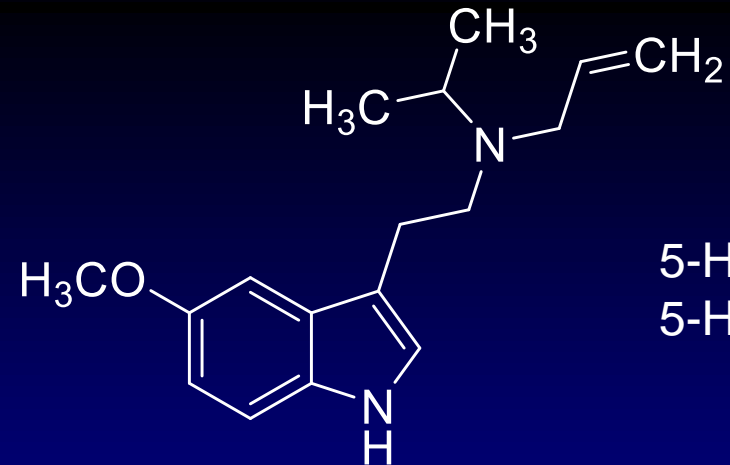
5-HT_{2A} = 462 nM
5-HT_{2B} = 2545 nM

iPALT



5-HT_{2A} = 219 nM
5-HT_{2B} = 59 nM

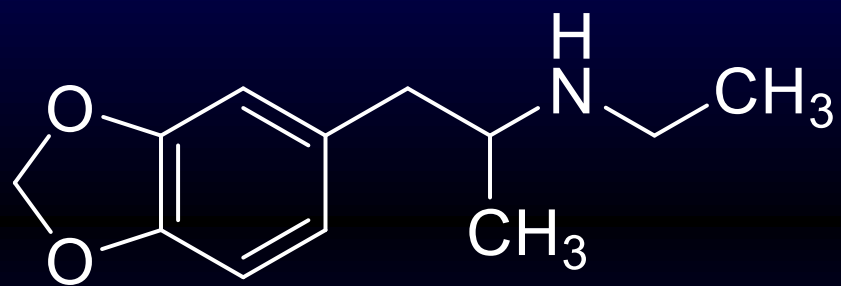
5-MeO-DALT



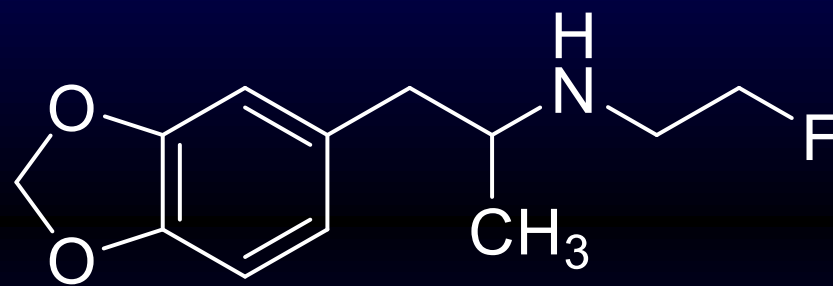
5-HT_{2A} = 10 nM
5-HT_{2B} = 87 nM

5-MeO-iPALT

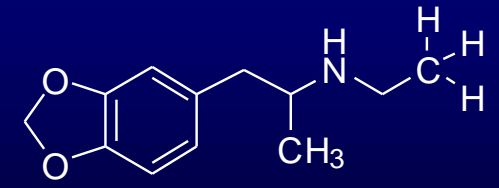
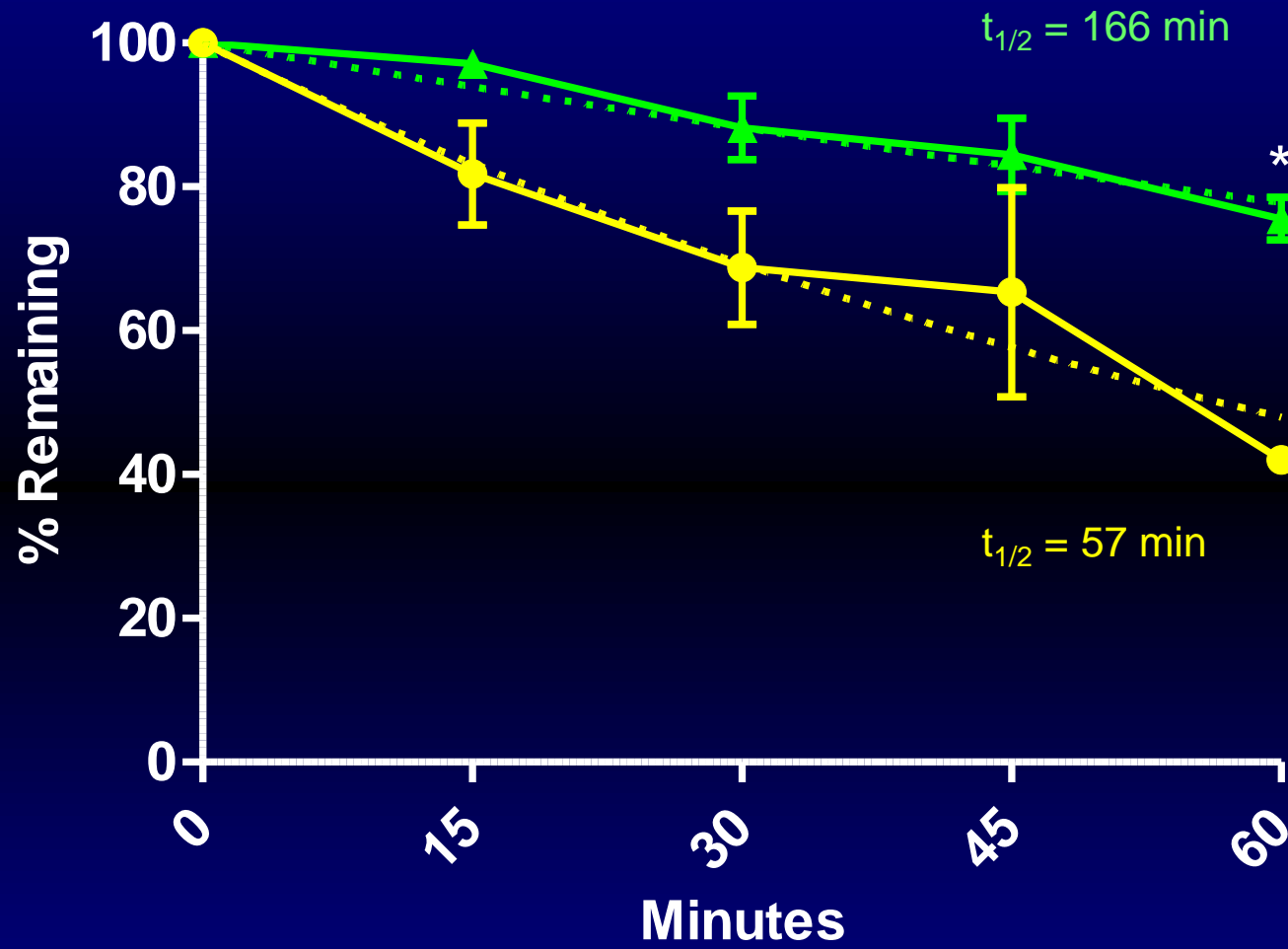
Chemical structures and binding affinities of some allyltryptamines



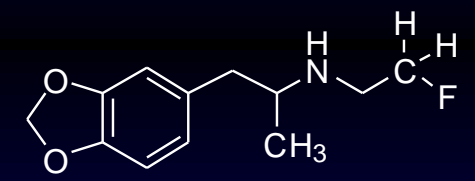
MDEA



MDEA-F

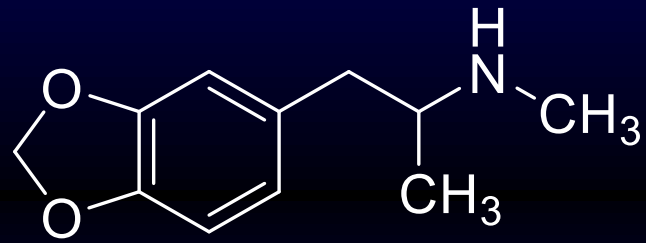


—▲— MDEA

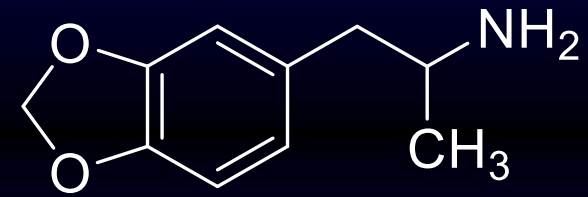


—●— MDEA-F

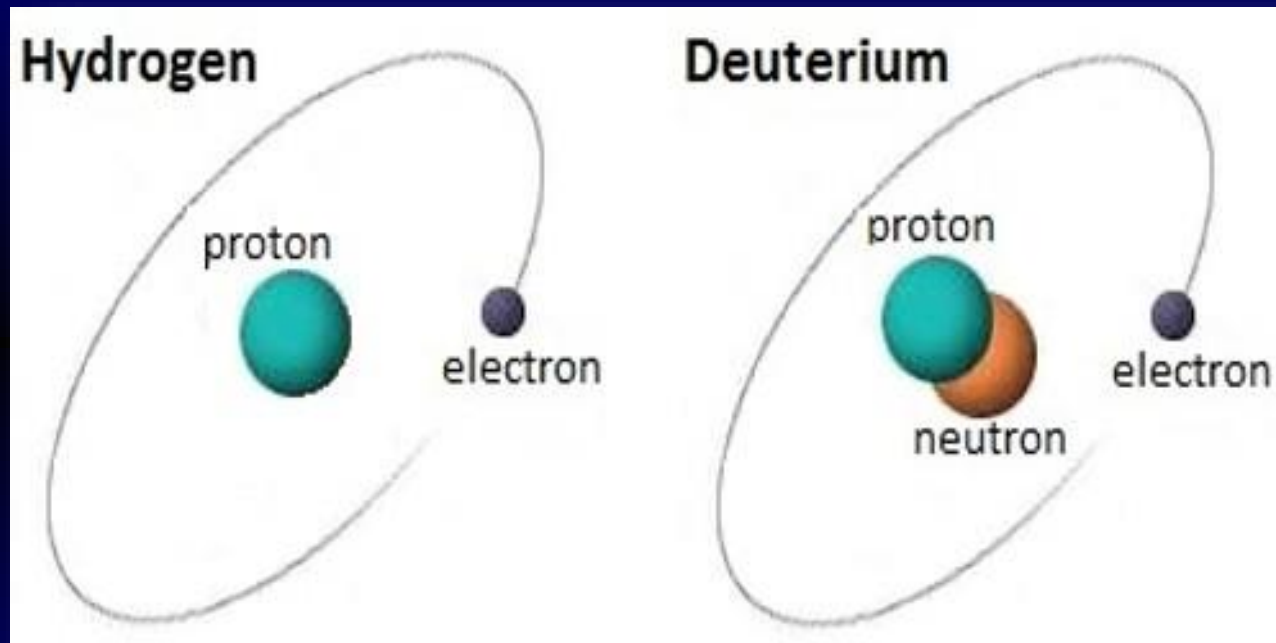
Metabolism by human liver microsomes

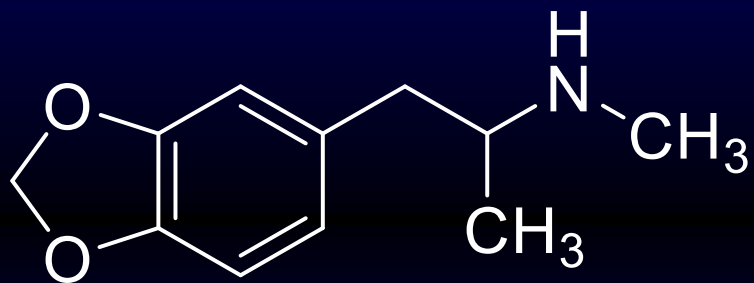


MDMA



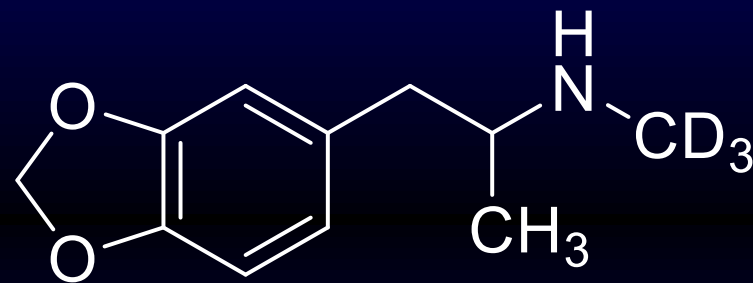
MDA





MDMA

$t_{1/2} = 393$ min



MDMA-*d*3

$t_{1/2} = 590$ min

Acknowledgements

- Paul Daley, Ph.D.
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Thank you!