OPEN ACCESS Freely available online

Organic Chemistry: Current Research

Perspective

Brief Note on Chemistry and Clinical Significance of Tricyclic Antidepressants (TCAs)

Nath Hook*

Department of Computational Chemistry and Drug Design, Peking University Shenzhen Graduate School, Shenzhen, China

DESCRIPTION

Tricyclic Antidepressants (TCAs) are a class of psychoactive drugs used primarily to treat clinical depression and other mood disorders. They are called "tricyclic" because of their common structural feature of three interconnected rings in their molecular structure. TCAs have been in use since the 1950s and were among the first medications developed to treat depression. While they are still prescribed, newer classes of antidepressants, such as selective Serotonin Reuptake Inhibitors (SSRIs) and Serotonin-Norepinephrine Reuptake Inhibitors (SNRIs), have become more popular due to their favorable side effect profiles. TCAs work by increasing the levels of certain neurotransmitters, particularly serotonin and norepinephrine, in the brain. They achieve this by inhibiting the reuptake of these neurotransmitters, meaning they block the proteins that reabsorb them in the synaptic cleft, allowing them to remain active for longer periods.

Structural features of TCAs

Three-ring structure: All TCAs share a tricyclic structure, typically composed of two six-membered rings and one five-membered ring. The central ring is usually a nitrogen-containing heterocycle, such as a diazepine or a dibenzazepine.

Amine functional groups: Most TCAs have amine functional groups attached to the central ring, often in the form of secondary or tertiary amines. These amines play a crucial role in the drugs' pharmacological activity.

Chemistry of TCAs

Amitriptyline: Amitriptyline is a TCA with the chemical name 3-(10,11-dihydro-5H-dibenzo[a,d][7]annulen-5-ylidene)-N,N-dimethylpropan-1-amine.Its core structure consists of a tricyclic ring system with a diazepine ring fused to two benzene rings. It has an amine functional group attached to the tricyclic structure, which contributes to its pharmacological activity. Amitriptyline is administered as its hydrochloride salt in medicinal formulations.

Imipramine: Imipramine is another TCA with chemical name 3-(10,11-dihydro-5H-dibenzo[b,f]azepin-5-yl)-N,N-dimethylpropan-1-amine. Like amitriptyline, imipramine has a tricyclic ring structure with a diazepine ring fused to two benzene rings. It also contains an amine functional group. Imipramine is available in various salt forms for medicinal use, including the hydrochloride salt.

Nortriptyline: Nortriptyline is a TCA and is actually a metabolite of amitriptyline. Its chemical name is (E)-3-(10,11-dihydro-5H-dibenzo[b,f]azepin-5-yl)-N-methylprop-2-en-1-amine. Nortriptyline shares the tricyclic ring structure with amitriptyline and imipramine but has a slightly different side chain. It contains an amine functional group in the side chain. Like the others, nortriptyline is also available as its hydrochloride salt for medicinal purposes.

Mechanism of action

TCAs exert their antidepressant effects by inhibiting the reuptake of neurotransmitters, such as serotonin and norepinephrine, in the synaptic cleft. By blocking the reuptake transporters, TCAs increase the levels of these neurotransmitters in the brain, which can help improve mood and alleviate depressive symptoms. TCAs also exhibit antagonistic effects on various receptors, including histamine H_1 receptors, α_1-adrenergic receptors, and muscarinic acetylcholine receptors. These interactions can lead to side effects, such as sedation, orthostatic hypotension, and anticholinergic effects. Some TCAs are chiral compounds, meaning they have non-superimposable mirror-image forms (enantiomers). The enantiomers of TCAs can exhibit different pharmacological properties and side effects. TCAs are metabolized in the liver by various cytochrome P450 enzymes. The metabolism can lead to the formation of active and inactive metabolites. The resulting metabolites are often excreted through the kidneys.

Correspondence to: Nath Hook, Department of Computational Chemistry and Drug Design, Peking University Shenzhen Graduate School, Shenzhen, China, E-mail: hook@nath.ac.il

Received: 15-Sep-2023, Manuscript No. OCCR-23-27922; **Editor assigned:** 18-Sep-2023, PreQC No. OCCR-23-27922 (PQ); **Reviewed:** 04-Oct-2023, QC No. OCCR-23-27922; **Revised:** 12-Oct-2023, Manuscript No.OCCR-23-27922 (R); **Published:** 20-Oct-2023, DOI: 10.35841/2161-0401.23.12.340.

Citation: Hook N (2023) Brief Note on Chemistry and Clinical Significance of Tricyclic Antidepressants (TCAs). Organic Chem Curr Res. 12:340.

Clinical significance

While TCAs are still used in certain clinical situations, they are not typically the first choice for treating depression. Newer antidepressant classes like SSRIs and SNRIs are favored due to their improved safety profiles and reduced side effects. However, TCAs may be considered when other treatments have failed or when their specific side effects may be beneficial for the patient's condition, such as in the management of neuropathic pain. Patients taking TCAs should be closely monitored by healthcare professionals, and individuals should not discontinue or change their medication regimen without consulting a healthcare provider due to the risk of withdrawal symptoms and potential relapse of depressive symptoms.

CONCLUSION

It's important to note that while TCAs can be effective in treating depression, they have significant side effects and potential for overdose, making them less favored as a first-line treatment compared to newer antidepressant classes like selective Serotonin Reuptake Inhibitors (SSRIs) and Serotonin-Norepinephrine Reuptake Inhibitors (SNRIs). TCAs are typically prescribed when other treatments have not been successful or when their specific side effects may be beneficial for the patient, such as for pain management in conditions like neuropathic pain. Patients taking TCAs should be closely monitored by healthcare professionals due to their potential for adverse effects and interactions. Moreover, these medications can have cardiac effects, such as potential arrhythmias, and can lead to orthostatic hypotension (a sudden drop in blood pressure upon standing). Therefore, their use requires careful consideration and monitoring by healthcare professionals.