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Drug Targeting Consider a Lead for Drug Discovery for Example Drug Antagonists

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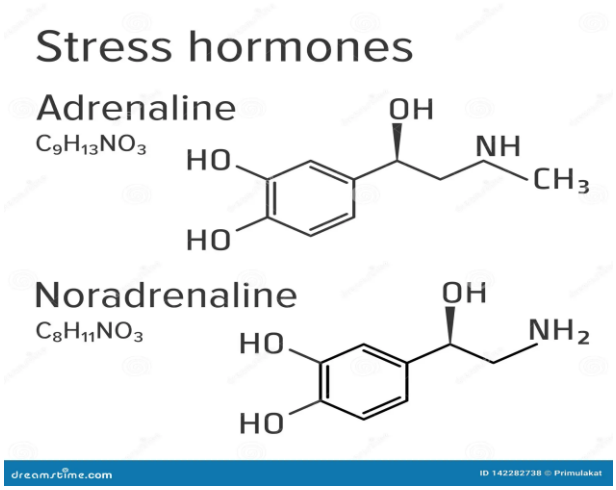
Abstract

The adrenergic compounds are chemical structures related to Adrenaline and Noradrenaline e.g., isoprenaline and terbutaline, when want to change in the chemical structure of adrenergic will lead us to an adrenergic blocking agents e.g., Alpha blockers and Beta blockers (prazosin, terazosin, propranolol and atenolol). Also, cholinergic agents especially direct cholinergics are chemical structures related to Acetylcholine which when manipulate of the Ach. We obtain anti-cholinergic agents like neostigmine, physostigmine, pilocarpine… etc. All the blockers are examples of drug discovery depends on Drug targeting (Alpha receptor, Beta receptor, Muscarinic receptor, Nicotinic receptor).

Keywords: adrenergic, adrenergic blockers, alpha blockers, beta blockers, cholinergics, anti-cholinergic, drug targeting, drug discovery

1. Introduction

The adrenaline act on alpha and beta receptor, while the noradrenaline act mainly on alpha receptors. The chemical structure of adrenaline and noradrenaline contain benzene ring and amine group and distance ethylene group. We note that the amine group when carrying methyl group (adrenaline) became act on alpha and beta receptors, while noradrenaline acts on alpha receptors mainly more than beta. So, the amine group when carry alkyl group, this alkyl called beta directing group for example terbutaline and isoprenaline.



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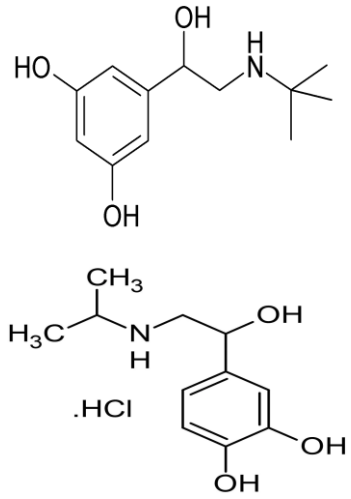

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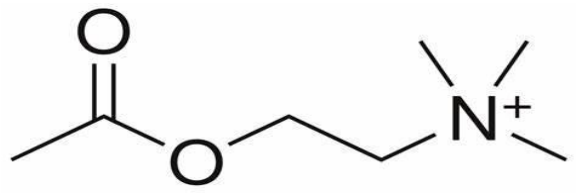
From the previous information, we noted the beta directing group is necessary for action on beta receptors which led us beta blocking agents, e.g., Non selective and selective beta blockers which are actually drug discovery, the acetyl choline is cholinergic drug which acts on muscarinic and nicotinic receptors, the acetyl choline structure contains acetate, and amine group and distance ethylene bridge, when change acetate into amide will act as direct cholinergic drug when substitute the ethylene bridge and other changes in other positions of acetylcholine obtained on cholinergic drugs act directly on cholinergic receptors, which may be give others pharmacological action such as physostigmine in Al-Alzheimer. When manipulate on the chemical structure of acetyl choline will lead to anti cholinergics which is actually drug discovery.



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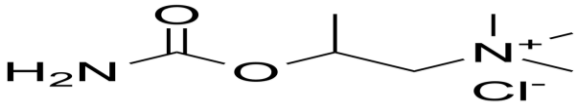

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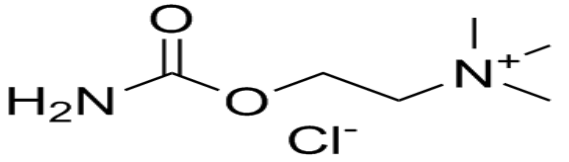

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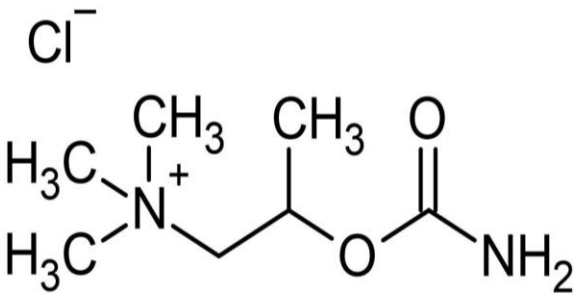

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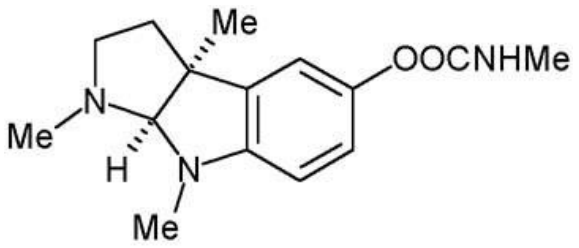

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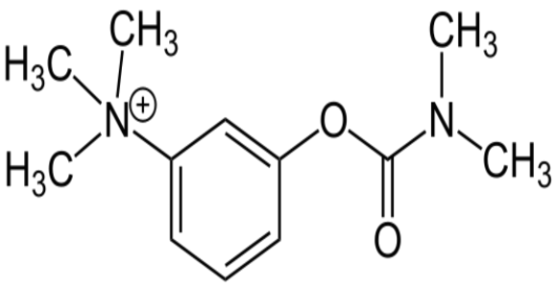

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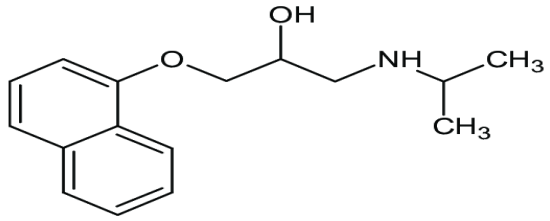
2. Chemistry and Pharmacology

Beta blockers and anti cholinergics which are drug discovery from drug targeting principles.

Nonselective beta blockers which act on beta -1 and beta -2 and block them, which used in hypertension, angina… etc. but contraindicated in bronchial asthma.



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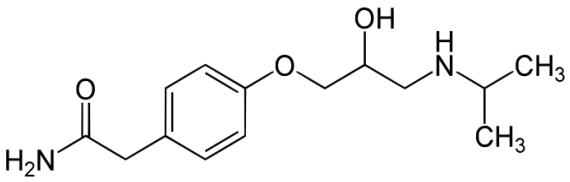
Comparison between propranolol and adrenaline revealed that the benzene ring becomes naphthalene and ethylene bridge of adrenaline becomes four atoms on naphthalene of propranolol, the beta directing group on propranolol (isopropyl group) larger than methyl of adrenaline.



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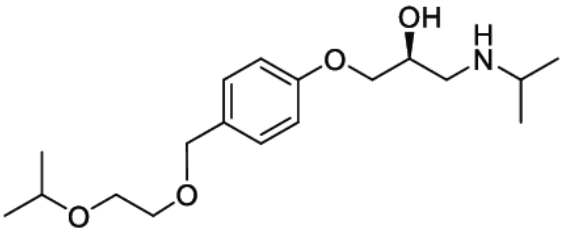

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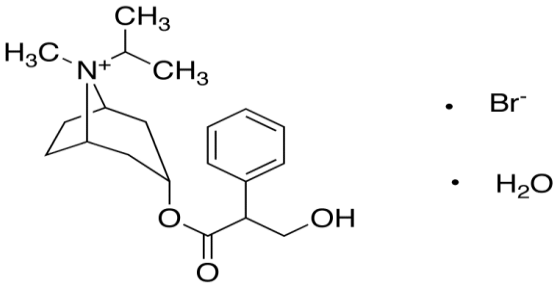
Atenolol, Bisoprolol and all selective beta-1blocker are examples of drug discovery where the chemical of beta one blocker similar of adrenaline where benzene ring present, distance between benzene and amine but longer and amine group present which carries beta directing group (isopropyl), from the previous we resulted the drug targeting are important for drug discovery, where we able to change some of groups, which may act on the same receptor or block these receptor and the others (isoprenaline and propranolol, atenolol and bisoprolol).

The anticholinergic drugs which block the muscarinic and nicotinic receptors are ipratropium bromide, propantheline bromide, orphenadrine citrate and biperiden, hexamethonium, decamethonium and succinyl choline.



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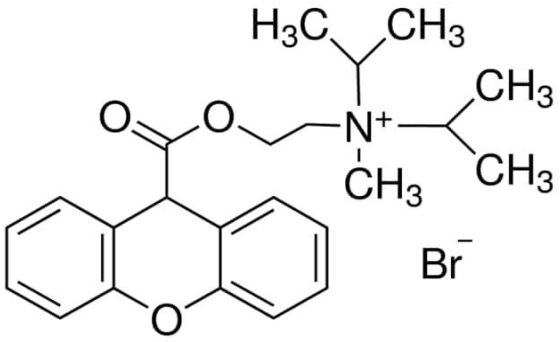

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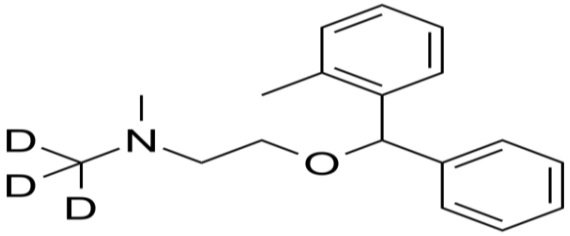

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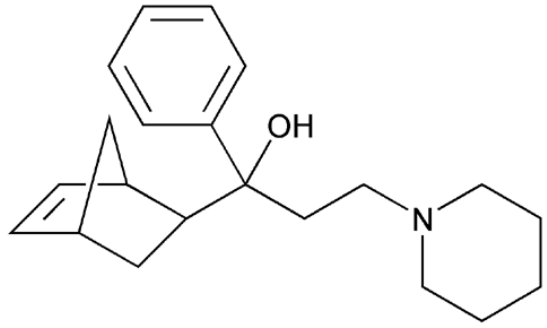

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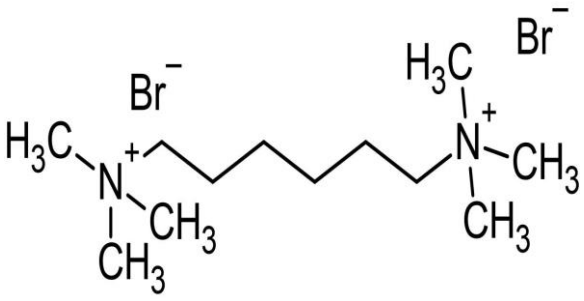

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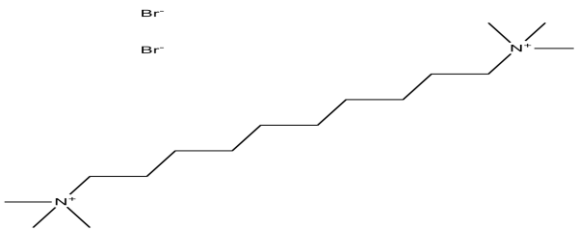

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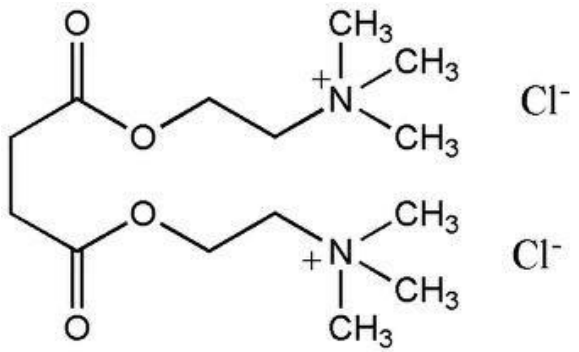

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The previous compounds are derived from acetylcholine but antagonize the action of it. Ipratropium compound is derived from atropine which antagonize Ach on muscarinic receptor via study of its structure it contains the acetate group and amine group attached by distance like Ach, when introduce of isopropyl group on nitrogen of atropine resulted ipratropium which antagonize Ach and produce bronchodilatation so used in bronchial asthma.

Propantheline bromide contains the features of chemical structures of Ach and used in treatment of gastritis, hypermotility of bladder, spasm (anticholinergic).

Orphenadrine citrate contains chemical parts like Ach which are used as Anti histaminic and central muscle relaxants and symptomatic treatment of parkinsonism.

Biperiden, it likes chemical structure of Ach, anti cholinergic used in treatment of parkinsonism, all the previous compounds act on muscarinic receptor but antagonize the action of Ach.

Hexamethonium, decamethonium and succinyl choline are similar in chemical structure of Ach which antagonizes action of Ach on neuromuscular junction and nicotinic receptors.

3. Conclusion

This article provides valuable insights into the principles of drug targeting and their application in drug discovery. It highlights how the chemical structures of key endogenous compounds like adrenaline, noradrenaline, and acetylcholine can serve as starting points for the development of various classes of therapeutic agents.

The article demonstrates how subtle modifications to the core chemical structures, such as the introduction of beta-directing groups or changes to the acetate moiety, can transform these endogenous compounds into antagonists that selectively target specific receptor subtypes. This targeted approach to drug design has been instrumental in the discovery of important drug classes like alpha blockers, beta blockers, and anticholinergic agents.

The detailed comparisons between the structures of lead compounds like adrenaline, propranolol, and ipratropium provide clear examples of how structural insights can guide the rational design of new drug candidates. This structure-activity relationship analysis is a fundamental aspect of modern drug discovery.

Overall, this article effectively illustrates the power of drug targeting strategies in the identification and development of novel pharmacotherapies. By leveraging our

understanding of endogenous signaling pathways and their associated receptor systems, medicinal chemists can systematically explore chemical space to uncover new drug candidates with improved selectivity and therapeutic potential.

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