PIONEER
ACADEMIC PUBLISHING LIMITED

Journal of Progress in Engineering and Physical Science
ISSN 2709-4006
www.pioneerpublisher.com/jpeps
Volume 4 Number 1 February 2025

The Direct Adrenergic Drugs Are Mostly Stereoselective for the Adrenergic Receptors

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doi:10.56397/JPEPS.2025.02.02

Abstract

The adrenaline, nor-adrenaline, and its analogs for example terbutaline, salbutamol, dipivefrin, ephedrine, phenylpropanolamine, phenylephrine… etc.

These compounds are characterized by containing chiral carbon which is surrounded by 4 different groups and makes these compounds able to rotate to the right or left which binds with adrenergic receptors in a specific position to make stereoselectivity between compounds and adrenergic receptors, this stereoselectivity increases the affinity of drug to the receptor and mostly increase the activity.

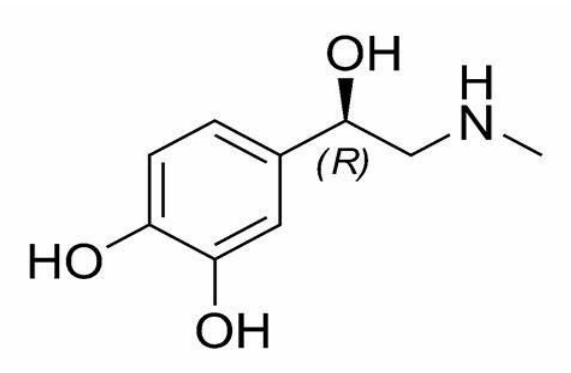
Keywords: adrenaline, nor-adrenaline, salbutamol, terbutaline, dipivefrine, ephedrine, adrenergic receptors, stereoselectivity

1. Introduction

Direct adrenomimetics are the drugs that act on the adrenergic receptors and stimulate the alpha receptor and beta receptor present in the body which increase the heart rate to keep the rhythm of the heart and stimulate the beta receptor to open the airways in the bronchi. These compounds to act on the receptors must have the chiral carbon center which binds with the adrenergic receptors, from the pharmacological activity of direct adrenomimetics we note the importance of the effect of adrenomimetics especially in the heart or bronchi, this pharmacological activity resulted from the good affinity of adrenergic receptors to give the activity of these compounds.

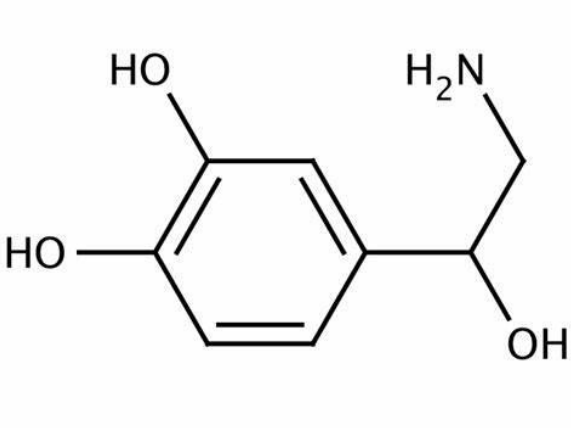
N.B. The chiral carbon of these compounds rotates to levo or dextro, so the compounds are either dextro or levo and may be in a racemic mixture (dextro and levo).

2. Chemistry and Pharmacology

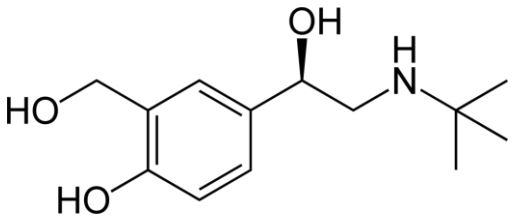


Adrenaline or epinephrine is an endogenous hormone that keeps the blood pressure present in a normal state and relieves bronchospasm.

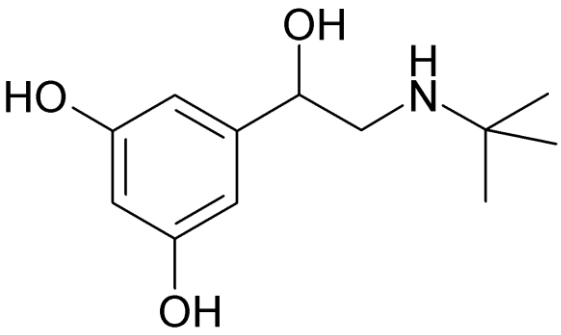
The chiral carbon of adrenaline makes it stereoselective for alpha and beta receptors, the adrenaline has a methyl group on the amino group which is beta beta-beta-directing group making the compound act on alpha and beta receptors.



Nor-adrenaline is an endogenous compound that is converted to adrenaline by methylation or metabolite of adrenaline by alkylation not contain beta directing group i.e. (the amino group does not carry methyl group), hence neither adrenaline nor norepinephrine acts mainly on alpha-adrenergic receptors, nor adrenaline containing chiral carbon which is highly selective for the adrenergic receptor and has stereoselectivity which increases the affinity following by good activity.

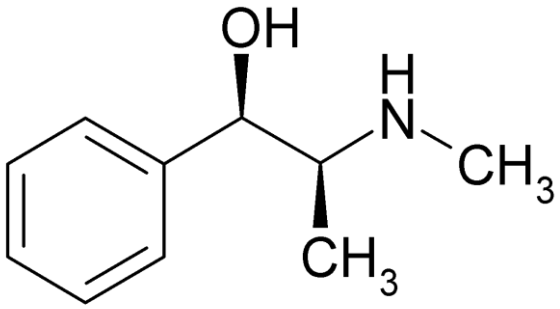


Salbutamol is characterized by stereoselectivity due to 3ry group on the amino group (beta directing group) and the presence of chiral carbon, these characteristics give selectivity and affinity to the beta-2 specific which is present in the bronchi and cause broncho dilatation in the treatment of bronchial asthma.



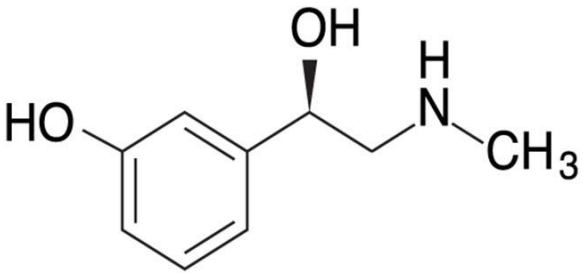
Terbutaline is a specific beta-2 agonist because it contains 3ry butyl group on the amino group and also it has chiral carbon which is a stereoselective compound to bind to the receptor in a good affinity and hence good activity, due to the stereoselectivity of this compound and beta-2 receptor.

N.B. This compound is not degraded by COMT (Catechol O-Methyl Transferase).

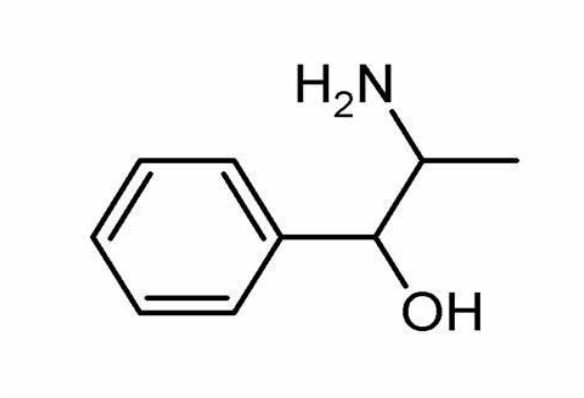


Ephedrine is a sympathomimetic drug that acts directly and indirectly, used to stimulate the respiratory center in the CNS, where it is a CNS stimulant and used to prevent hypotension

during anesthesia, this compound has 2 chiral centers which can be classified as erythro and threo, this compound exhibit stereoselectivity when acting as a direct adrenomimetic.



Phenylephrine is an adrenergic compound that acts on alpha receptors and is used medicinally as a decongestant in nasal congestion, this compound contains chiral carbon which makes it have stereoselectivity to alpha-adrenergic receptors.



Phenylpropanolamine is a stereoselective compound where it contains 2 chiral carbons that act on alpha-adrenergic receptors and are used medicinally in the treatment of nasal congestion, this stereoselectivity of the compound makes a good affinity to receptors resulting in good activity.

3. Conclusion

This article outlines the importance of stereoselectivity in the pharmacological efficacy of direct adrenergic drugs, highlighting the relationship between molecular structure and receptor interaction.

The stereoselectivity of direct adrenergic drugs plays a crucial role in their pharmacological effectiveness. The presence of chiral carbons in compounds such as adrenaline, noradrenaline, salbutamol, terbutaline, ephedrine, phenylephrine, and phenylpropanolamine significantly influence their affinity for adrenergic receptors. This stereoselectivity not only enhances the binding efficacy of these drugs but also contributes to their therapeutic outcomes, particularly in cardiovascular and respiratory treatments. Understanding the relationship between chiral structures and receptor interactions is essential for the development of more selective and effective adrenergic agents. Future research should continue to explore the implications of stereochemistry in drug design, aiming to optimize therapeutic efficacy while minimizing side effects.