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A Review on Some Catechol Containing Inotropes: Drugs

C. S. Patil, Sanjeevan A. Survase, Yogesh N. Bharate, Mahadeo A. Sakhare, Kuldeep B. Sakhare
Department of Chemistry, Shri Muktanand College, Gangapur, Dist. Chh. Sambhajinagar, Maharashtra, India
Department of Chemistry, Balbhim Arts, Science & Commerce College, Beed, Maharashtra, India

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ABSTRACT

Inotropes are the medications that are used to beat or contract heart muscles with more efficient or less efficient, depending on whether it's a positive or negative inotrope. Positive inotropes strengthen the force of the heartbeat and can assist when heart can't get sufficient blood to body because it is too weak to pump the sufficient amount of blood to body needs. Positive inotropes improves heart muscle contractions, raising cardiac output to a normal level and increasing the amount of blood, heart can pump out. Inotropes act on cardiomyocytes, the cells in heart muscle. In present review we have collected information of Dopamine, Dobutamine, Adrenaline, Nor-Adrenaline regarding their uses, absorption, half-life, mechanism of action, adverse effects, drug interaction etc.

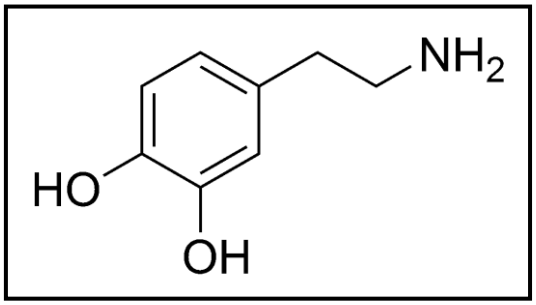
Keywords: Dopamine, Dobutamine, Adrenaline, Nor-Adrenaline.

Introduction

Inotropic state is most often used in reference to number of drugs that affect the activity of heart muscle, it can also refer to pathological conditions. Inotropes are used in the management of various cardiovascular conditions. The choice of drugs depends on pharmacological effects of individual agents with respect to the condition. Positive inotropic drugs help to improve heart beats with more force while negative inotropic drugs lowers the heart muscles activity to contract with less force. [1-2]. One of the important factor that affect inotropic state is the concentration of calcium in the cytoplasm of the muscle cell. Positive inotropes increase this level, while negative inotropes decrease its level but it is not applicable for all inotropic drugs due to their differential mechanism for manipulating the calcium level. By increasing the concentration of intracellular calcium or increasing the sensitivity of receptor proteins to calcium, positive inotropic agents can increase myocardial contractility [3-5]. Calcium can pass through L-type calcium channel and T-type calcium channel. L-type channels are important in maintaining an action potential, while T-type channels are important in initiating them [6].

Positive inotropic agents:

Dopamine:



Uses: It is a vasostimulant used to treat low blood pressure, low heart rate, and cardiac arrest. Low infusion rates act on the visceral vasculature to produce vasodilation, including the kidneys. [7-8].

Absorption: It is rapidly absorbed in the small intestine and its Biotransformation proceeds very rapidly with major excretion products 3-4-dihydroxy-phenylacetic acid and 3-methoxy-4-hydroxy-phenylacetic acid.

Metabolism: It is metabolized via methylation by catechol-o-methyl-transferase and via deamination by monoamine oxidase A. Both MAO-A and MAO-B effectively metabolize dopamine.

Excretion: It is excreted in urine, the main end-product is homovanillic acid (HVA). From the bloodstream, homovanillic acid is filtered out by the kidneys and then excreted in the urine [9].

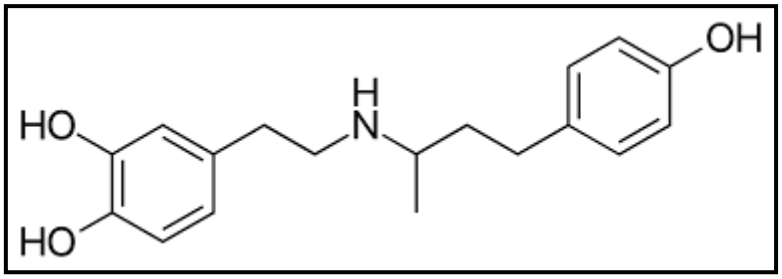
Half-life: It's onset of action starts within 5 min. after intravenous administration, with plasma half-life about 2 min.

Mechanism of action: It is a precursor to norepinephrine in noradrenergic nerves and also a neurotransmitter in certain areas of CNS, It produces positive chronotropic and inotropic effects on the myocardium, resulting in increased heart rate and cardiac contractility. It is accomplished directly by exerting an agonist action on beta-adrenoceptors and indirectly by causing release of norepinephrine from storage sites in sympathetic nerve endings. In the brain, dopamine acts as an agonist to the five dopamine receptor subtypes D1, D2, D3, D4, D5 [10].

Adverse effects: Chest pain, shortness of breath, feeling cold, lightheadedness, blue discoloration of hands and feet etc.

Drug interactions: It may interact with vasopressin, epinephrine, droperidol, haloperidol, midodrine, diuretics, phenytoin, beta blockers, antidepressants, ergot medicines, phenothiazines, MAO inhibitors, selegiline, linezolid etc [11].

Dobutamine:



Uses: It is used in treatment of heart failure, cardiac decompensation, it helps to strengthen the heart muscle. It stimulates heart muscle and improves blood flow [12-13].

Metabolism: It is readily metabolised by COMT in the liver, the principal routes of metabolism are methylation of the catechol and conjugation.

Excretion: It is excreted in urine, the major excretion products are the conjugates of dobutamine and 3-O-methyl dobutamine.

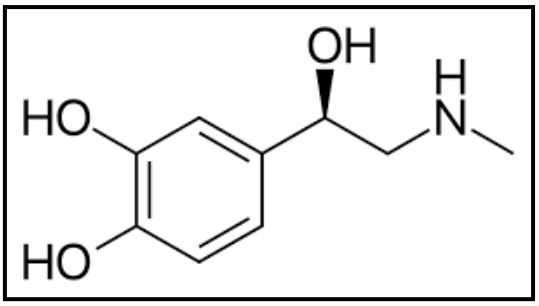
Half-life: about 2-3 minutes.

Mechanism of action: It directly stimulates β-1 receptors of the heart to increase myocardial contractility and stroke volume, resulting in increased cardiac output. Its inotropic effects on the myocardium occur by selectively binding and activating the β-1 receptors which increases contractility, leading to decreased end-systolic volume and, therefore, increased stroke volume [14].

Adverse effects: Weakness, headache, dizziness, increased heart rate, trouble in speaking or walking etc

Drug interactions: It is contraindicated for concomitant use with dihydroergotamine leading to synergistic effects or phenelzine leading to additive effects. Both combinations may increase the risk of severe hypertension [15].

Adrenaline:



Uses: It belongs to a group of medicines used for the treatment of serious shock produced by a severe allergic reaction (anaphylaxis). It may also be used to restart heart if it has stopped. It may also be given in different forms during cardiac arrest, croup and asthma [16].

Absorption: By subcutaneously it is rapidly absorbed, probably by lymphatic channels.

Metabolism: It stimulates ketogenesis, lipolysis, thermogenesis, glycolysis and raises plasma glucose concentrations by stimulating glycogenolysis and gluconeogenesis. Metabolism is primarily in the liver, along with kidneys, skeletal muscle and mesenteric organs. It is degraded into an inactive metabolite vanillylmandelic acid by MAO and COMT and excreted into the urine.

Excretion: It is excreted in urine, excretion products are metanephrine and normetanephrine.

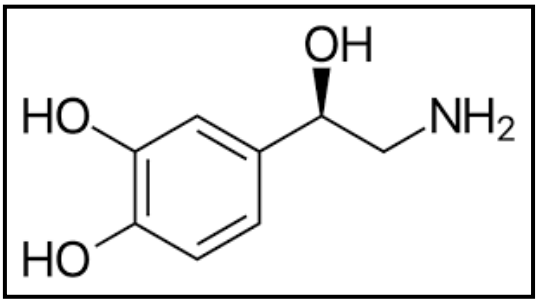
Half-life: Plasma half-life is about 2- 3 minutes.

Mechanism of action: It is a nonselective agonist of all adrenergic receptors, including the major subtypes α_1, α_2, β_1, β_2, and β_3. It acts on α_1 receptors, epinephrine induces increased vascular smooth muscle contraction, pupillary dilator muscle contraction, and intestinal sphincter muscle contraction. High levels of adrenaline cause smooth muscle relaxation in the airways but causes contraction of the smooth muscle that lines most arterioles.

Adverse effects: Hypertension, anxiety, tachycardia, palpitations, headache, diaphoresis, nausea, vomiting, weakness etc

Drug interactions: It may interact with digoxin, diuretics, levothyroxine, chlorpheniramine, beta-blockers, antidepressants, ergot medicines and MAO inhibitors.

Nor-Adrenaline:



Uses: It is both a neurotransmitter and a hormone and plays an important role in body's fight-or-flight response. It is used to increase and maintain blood pressure in limited, short-term serious health situations. Also used to treat hypotension (low blood pressure) that may occur with certain medical conditions or surgical procedures.

Metabolism: It is metabolized in the liver and other tissues by enzymes catechol-O-methyltransferase (COMT) and MAO with major metabolites normetanephrine and vanillylmandelic acid.

Excretion: It is excreted in urine, major metabolites are normetanephrine and vanillylmandelic acid.

Half-life: By intravenous administration about 1 to 2 minutes.

Mechanism of action: It predominantly stimulates α_1 receptors to cause peripheral vasoconstriction and increase blood pressure. It also acts on β-1 adrenergic receptors, causing increase in heart rate and cardiac output [17].

Adverse effects: Headache, shortness of breath, anxiety, dizziness, irregular heartbeat, urinary retention, blurred vision etc.

Drug interactions: It may interact with monoamine oxidase inhibitors or amitriptyline and imipramine-type antidepressants.

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