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A REVIEW ON NEW ANTIHYPERTENSIVE AGENT: IRBESARTAN

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Abstract

Hypertension is currently measure disorder obtain in the world population. Irbesartan is classified as an angiotensin II receptor type 1 antagonist. Angiotensin II receptor type 1 antagonists are widely used in treatment of diseases like hypertension, heart failure, myocardial infarction and diabetic nephropathy.The clinical and pharmacological analysis of this drug givesidea about effectivity of this drug in hypertension condition.Irbesartan act on renin angiotensin system and decreases biding of angiotensin to the receptor so decreases the blood pressure and act as an antihypertensive agent. Irbesartan is tetrazole derivative which selectively inhibit or antagonise the angiotensin type II receptor. In this review gives detail about mechanism of action of irbesartan in hypertension.

Keywords:

Irbesartan, Hypertension, Anti hypertensive drug, Angiotensin ii receptor antagonist.

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INTRODUCTION

Irbesartan is the drug used in hypertension, angina pectoris, cardiac artery disorder, heart failure like cardiac disorder. Irbesartan an angiotensin II receptor antagonist, is used mainly for the treatment of hypertension.[1] It is an orally active nonpeptidetetrazole derivative. IUPAN name of Irbesartan is 2-butyl-3-({4-[2-(2H-1,2,3,4-tetrazol-5-yl)phenyl]phenyl}methyl)-1,3-diazaspiro[4.4]non-1-en-4-one.[2] These are organic compounds containing a biphenyl attached to a tetrazole (Table 1). A carbon atom of the biphenyl moiety is boned to a carbon or the nitrogen atom of the tetrazole moiety so it's highly selective for angiotensin II receptor.

Table:1 Structural and introductionofIrbesartan[3]

Serial number	Class	Identification
1	Primary class	Organic compound
2	Superclass	Heterocyclic Compound
3	Class	Azoles
4	Subclass	Tetrazole derivative
5	Direct parent	Biphenyltetrazoles and Derivatives
6	Alternative parent	Biphenyls and Derivatives; Imidazolinones; Tertiary Carboxylic Acid Amides
7	Minimum dose	150mg
8	Maximum dose	350mg
9	Single drug brand	Xarb, irbestin
10	Combination brand	Xarb – H, Irbe – H

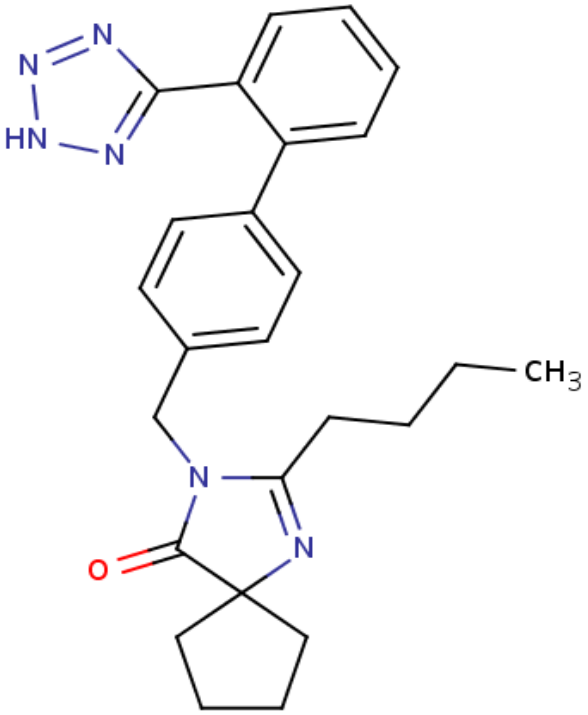

Figure: 1 Structure of Irbesartan[4]

Appearance is white or almost white, crystalline powder. Solubility is given in practically insoluble in water, sparingly soluble in methanol, slightly soluble in methylene chloride, its also spiringly soluble in ethanol and acetonitrile. It shows polymorphism.

MECHANISM OF ACTION:

Irbesartan is a nonpeptidetetrazole derivative and an angiotensin II antagonist that selectively blocks the binding of angiotensin II to the AT1 receptor[1] In the renin-angiotensin system, angiotensin I is converted by angiotensin-converting enzyme (ACE) to form angiotensin II. Angiotensin II stimulates the adrenal cortex to synthesize and secrete aldosterone, which decreases the excretion of sodium and increases the excretion of potassium. Angiotensin II also acts as a vasoconstrictor in vascular smooth muscle. Irbesartan, by blocking the binding of angiotensin II to the AT1 receptor, promotes vasodilation and decreases the effects of aldosterone. The negative feedback regulation of angiotensin II on renin secretion is also inhibited, but the resulting rise in plasma renin concentrations and consequent rise in angiotensin II plasma concentrations do not counteract the blood pressure–lowering effect that occurs.Irbesartan is a specific competitive antagonist of AT1 receptors with a much greater affinity (more than 8500-fold) for the AT1 receptor than for the AT2 receptor and no agonist activity.

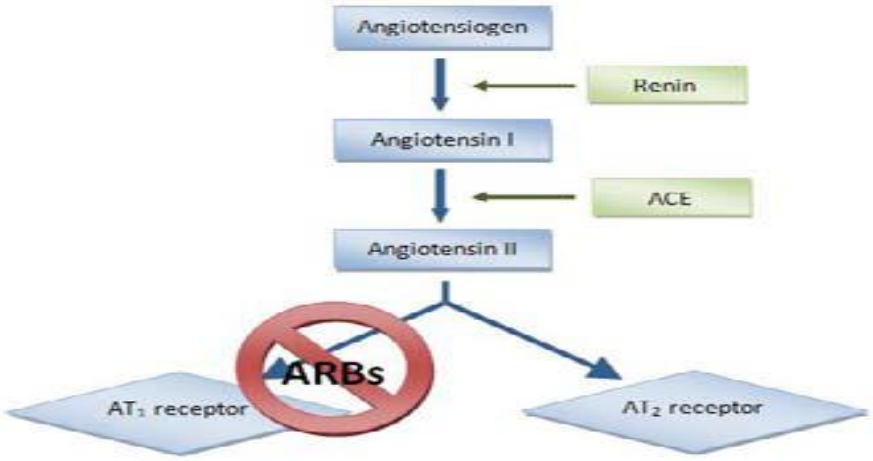

Figure:2 Mechanism of Irbesartan[5]

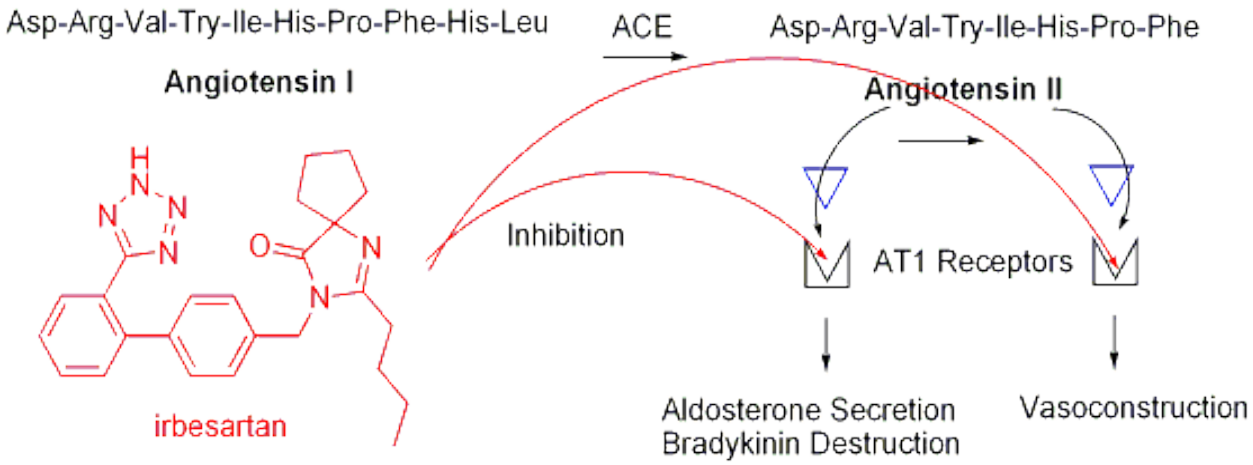

Figure 3: Chemical mechanism of Irbesartan[8]

Rapid and complete with an average absolute bioavailability of 60-80%. Food has no effect on bioavailability.it also used in diabetic nephropathy with an elevated serum creatinine and proteinuria (>300 mg/day) in patients with type 2 diabetes and hypertension. Irbesartan is also used as a second line agent in the treatment of congestive heart failure.[6]

The action of ARBs is different from ACE inhibitors, which block the conversion of angiotensin I to angiotensin II, meaning that the production of angiotensin II is not completely inhibited, as the hormone can be formed via other enzymes. Also, unlike ACE inhibitors, Irbesartan and other ARBs do not interfere with response to bradykinins and substance P, which allows for the absence of adverse effects that are present in ACE inhibitors (e. .g. dry cough)

CHEMICAL MECHANISM OF IRBESARTAN

Structure activity relationship is also affected the pharmacological mechanism of Irbesartan and the fuction group gives specific activity in the chemical mechanism and pharmacodynamics action of the drug. Chemical derivative is also gives effective change in mechanism of action[7]**.** The "acidic group" is thought to mimic either the phenol or the Asp1 carboxylate of angiotensin II. Groups capable of such a role include the carboxylic acid (A), a phenyl tetrazole or isostere (B), or a phenyl carboxylate (C). In the biphenyl series, the tetrazole and carboxylate groups must be in the ortho position for optimal activity. The n-butyl group of the model compound provides hydrophobic binding and, most likely, mimics the side chain of Ile5 of angiotensin II. As seen with azilsartan, candesartan, telmisartan, and olmesartan, this n-butyl group can be replaced with either an ethyl ether or an n-propyl group. The imidazole ring or an isosteric equivalent is required to mimic the His6 side chain of angiotensin II. Substitution can vary at the "R" position. A variety of R groups, including a carboxylic acid, a hydroxymethyl group, a ketone, or a Benz imidazole ring, are present in currently available ARBs and are thought to interact with the AT1 receptor through either ionic, ion–dipole, or dipole–dipole bonds.

Renin-angiotensin system is responsible for effects such as vasoconstriction, stimulation of synthesis and release of aldosterone, cardiac stimulation, and renal reabsorption of sodium[9]. Irbesartan inhibition of angiotensin II binding to the AT1 receptor leads to multiple effects including vasodilation, a reduction in the secretion of vasopressin, and reduction in the production and secretion of aldosterone. The resulting effect is a decrease in blood pressure.

CONCLUSION

Irbesartan is a potent, long-acting, nonpeptide angiotensin II receptor antagonist having high selectivity for the AT1 subtype (angiotensin I). It is potentially safe and more tolerable than other classes of antihypertensive drugs. Irbesartan is an effective antihypertensive agent in patients with mild to moderate hypertension. The drug also reduces blood pressure when used as monotherapy in patients with severe hypertension or when used adjunctively in patients with resistant hypertension. Importantly, Irbesartan appears to be as effective and well tolerated as other commonly used antihypertensive agents. The drug therefore represents a useful therapeutic option in the management of patients with hypertension will be particularly useful in patients not responding to, or intolerant of, anti-hypertensive agents from other drug classes. Irbesartan may be an appropriate choice for first-line treatment of patients with mild-to-moderate hypertension, heart failure, myocardial infarction and diabetic nephropathy.

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