Int J Pharm Bio Sci 2016 July; 7(3): (P) 81-83

Original Research Article **Pharmacology**

International Journal of Pharma and Bio Sciences **ISSN 0975-6299**

COMPARATIVE FREE RADICAL SCAVENGING ACTIVITY OF ANGIOTENSIN RECEPTOR BLOCKERS

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ABSTRACT

Angiotensin receptor blockers (ARBs) are used in various disease conditions such as hypertension, heart failure and diabetic nephropathy. Telmisartan, Valsartan are potent ARBs and specific competitive antagonist of angiotensin AT_1 receptors. Oxidative stress has a vital role in the pathogenesis of hypertension, diabetes mellitus, and cardiac failures. In this study, the antioxidant potential of Telmisartan and Valsartan was evaluated and compared using DPPH assay. It was found out that both these drugs have antioxidant properties and Valsartan has better antioxidant property than Telmisartan. In conclusion, the antioxidant property of the above ARBs could be beneficial in preventing complications in various disease conditions due to oxidative damage.

KEYWORDS: **Telmisartan,Valsartan,Oxidative stress,Antioxidant property.**

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INTRODUCTION

Angiotensin receptor blockers (ARB) competitively inhibit AT_1 receptor, thereby inhibit Angiotensin II (Ang II) action regardless of the biochemical pathway resulting in the formation of Ang II. AT_1 and AT_2 receptors are the two distinct receptors of Ang II[1]. ARBs have high affinity and more selective action on AT_1 receptor over AT_2 receptors. Stimulation of the AT_1 receptor leads to constriction of blood vessels, development of new blood vessels and promote cell reproduction. Whereas AT_2 receptor stimulation produce effects that are opposite to AT_1 stimulation such as vasodilatation, prevention of new blood vessel formation. Pharmacological studies indicate that the AT_2 receptor stimulation will oppose the effect of the AT_1[2]. Thus, AT_1 and AT_2 receptors maintain a balance between Nitric oxide (NO) and free radicals. Previous studies stated that Ang II act on AT_1 and cause free radical formation by stimulating non-phagocytic NADPH oxidase [3] . When AT1 receptors are blocked with ARBs, Ang II which are present in the circulation will act on AT_2 receptor and produce an effect opposite to AT_1 stimulation. ARBs are used in the treatment of hypertension, diabetic nephropathy, stroke prophylaxis, cardiac failure and to reduce cardiovascular mortality. Recently oxidative stress was proposed to be an important factor in the pathogenesis of various disease conditions. Hence in this study the antioxidant property of two ARBs are evaluated and compared using DPPH assay.

MATERIALS AND METHODS

DPPH (1,1-diphenyl, 2-picrylhydrazyl) was obtained from Sigma Chemical Co. CRC, Banglore. Ascorbic acid was obtained from SD Fine Chem.Ltd., Biosar, India.DPPH radical scavenging activity was done using the method of Yohozowa et al[4]. The reaction mixture containing 1.9 ml of DPPH solution (150µM in Ethanol) with different concentrations of the substances (50, 100, 200, 300, 400, 500µg/0.1ml) was shaken and incubated in dark for 20mins at room temperature. The resultant absorbance was recorded at 517nm. The percentage inhibition was calculated. The standard drug used was Ascorbic acid.

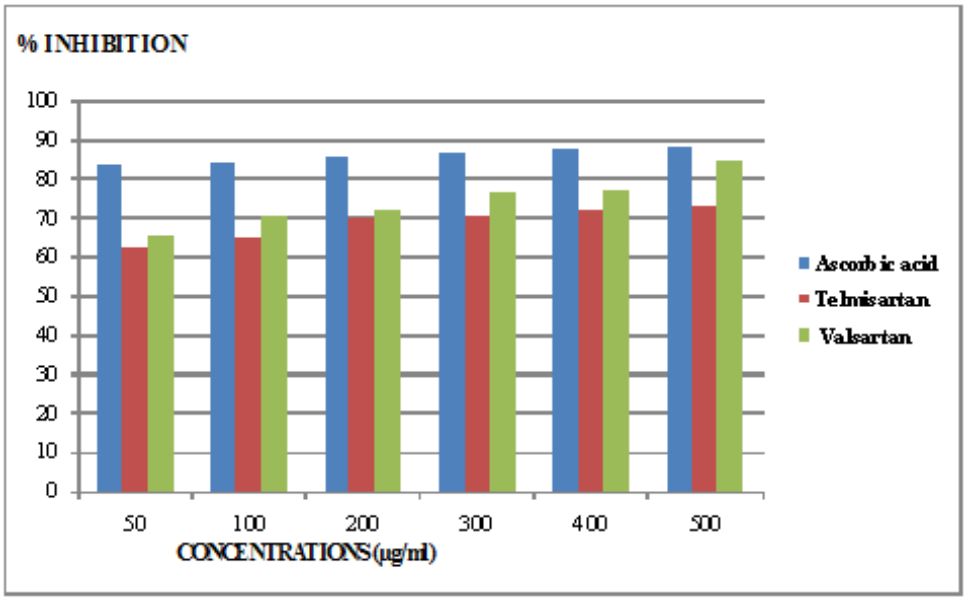
Table 1

% Inhibition By Telmisartan And Valsartan Against Standard Ascorbic Acid

CONCENTRATION (µg/0.1ml)	% INHIBITION		
	STD (ASCORBIC ACID)	Telmisartan	Valsartan
50	83.39±0.82	62.38±0.52	65.09±1.82
100	84.07±0.85	64.77±0.06	70.40±1.00
200	85.36±0.63	69.46±0.16	72.16±1.04
300	86.60±0.26	70.56±0.14	76.11±3.20
400	87.45±0.10	71.85±0.09	77.12±2.84
500	88.21±0.05	72.82±0.08	84.53±2.81

Figure 1

Bar Diagram Showing % Inhibition By Telmisartan And Valsartan Against Standard Ascorbic Acid



RESULTS AND DISCUSSION

From this study, the free radical scavenging activity showed that percentage of inhibition increases with increase in concentrations of both the drugs. This shows that both the drugs have significant antioxidant property. But Valsartan has better antioxidant property compared to Telmisartan. As Oxidative stress can accelerate tissue and vascular injury, drugs like ARBs with significant antioxidant property could have a vital role in the reduction of oxidative stress. Thereby may prevent the progression of various disease conditions and their complications like hypertension, diabetic nephropathy, cardiovascular morbities and mortalities. Oxidative stress is increased in human hypertension with the decrease in nitric oxide level [3] . Ang II stimulate the synthesis of superoxide anion and other free radicals by inducing endothelial nitric oxide synthase (eNOS) uncoupling. NO bioavailability is determined by these free radicals as they rapidly degrade NO[5]. Thus the balance shift towards increased free radical production with reduced NO , which can result in the development of hypertension. Evidences have suggested that high blood glucose levels can induce oxidative stress by various mechanisms [6,7]. In Hyperglycemia, nitroso-oxidant balance is lost and a pro-oxidant state exist which can lead to tissue and vascular injury. Free radicals produced can cause defect in insulin gene expression and insulin secretion, and also pancreatic β cell damage which can result in diabetes mellitus and its complications. Studies also suggest that steps to reduce oxidative damage can either prevent or slow down the progression of diabetic nephropathy[8]. Hyperglycemia-induced oxidative stress can cause endothelial dysfunction and can result in micro-vascular and macro-vascular diseases[6]. Previous data suggest that oxidative damage can induce structural and functional changes in the heart that can lead to disease progression[9]. In a failing myocardium free radical synthesis is increased. Thus ARBs by their antioxidant effect can prevent further damage to a failing heart. Studies have stated that Agtr1a gene encode for $AT_{1,}$ and knockout of this gene can prolong the life-span of mice by 26%, probably due to reduction of oxidative damage [10,11]. The ARBs may also produce the same effect by blocking AT_1 receptors. Oxidative damage play a vital role in the incidence and progression of Alzheimer's disease[12], hence ARBs by reducing the oxidative damage may prove useful in Alzheimer's disease. Since both these ARBs have significant free radical scavenging property, they may be more beneficial in the treatment and/or prevention of various disease conditions and complications due to oxidative damages. Further studies are required for definitive conclusion regarding the pleotropic effects of angiotensin receptor blockers.

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