IF : 4.547 | IC Value 80.26 Volume-6, Issue-3, March - 2017 • ISSN No 2277 - 8160

Original Research Paper Pharmacology

NECCESSITY OF ANTIHYPERTENSIVE DRUG AS ANTIOXIDANT IN HYPERTENSION: ACTION OF CARVEDILOL AS A SCAVENGER OF NITRIC OXIDE RADICALS

Dr.Brigida.S Department of Pharmacology, Sree Balaji Medical College and Research Hospital, Chrompet, Chennai-600044 Tamilnadu, India.

Dr.Muthiah.N.S Department of Pharmacology, Sree Balaji Medical College and Research Hospital, Chrompet, Chennai-600044 Tamilnadu, India.

ABSTRACT

Background: Hypertension is one among the leading disease causing morbidity and mortality irrespective of other co morbid conditions. Hypothetically the culprit behind has been the accumulation of free radicals causing oxidative stress. Oxidative stress plays a vital role in pathophysiological changes in hypertension. Prescribing 2 or 3 medications is one among the cause for major drug interaction and hence to prevent it, necessity of the pertained drug for the disease to act as a scavenger is the need of the hour in current scenario. **Objective:** In this study we are intended to find antihypertensive drug Carvedilol (3.125mg) percentage of scavenging action of nitric oxide radicals against the standard ascorbic acid and commercially available vitamin C. **Result:** It is found that the nitric oxide scavenging activity of Carvedilol (3.125) is quite appreciable (75.74%) when compared to ascorbic acid (98.5%) and Vit C(90.58%).

KEYWORDS : NITRIC OXIDE SCAVENGER, CARVEDILOL, ANTIOXIDANT IN HYPERTENSION

Introduction

Hypertension contributes to the pathophysiology of various diseases like renal failure, cardiovascular disease and cerebrovascular accident. Vascular remodeling, endothelial dysfunctions are few among those which contributes to the pathogenesis of hypertension and are basically due to oxidative stress caused by free radical accumulation. Among the free radicals producing oxidative stress, reactive oxygen species (ROS) and reactive nitrogen species (RNS) are the major culprit. These are responsible for the decreased nitric oxide bioavailability as well as decreased antioxidant capacity in vascular structures.

Reactive Nitrogen species and Oxidative stress

Direct scavenging of O_2^- towards $ONOO^-$ by NO is the antioxidant role of nitric oxide. NO is one of the biological molecule which can act against the free radical in vascular structures. Formation of $ONOO^-$ (PEROXYNITRITE) a free radical require no specific enzymes as it is faster than the enzyme superoxide dismutase(antioxidant). Consequently peroxynitrite at physiological PH equilibrates rapidly and forms highly reactive hydroxyl radical (HO^-). $ONOO^-$ has the capacity to interact with proteins, amino acids like cysteine, methionine, tryptophan and histidine oxidation, tyrosine nitration, lipids. Rapid conversion of peroxynitrite further produces highly reactive hydroxyl radical (HO^-) which aggravates endothelial damage and vascular derangements. Hence it is very essential for a scavenger to remove the free radical species, which is done by NO. But the non availability of NO at the blood vessels due to pathophysiological changes in hypertension further complicates by accumulating free radicals. Hence the anti hypertensive's which we are choosing if it not only addresses the pathology if it has antioxidant property will favor the prognosis in a positive way.

Carvedilol (3.125mg) and vitamin C

The test drug (Carvedilol (3.125mg)) is a potent α_1 adrenoreceptor antagonist , competitive β adrenoreceptor antagonist (a calcium channel antagonist at high concentration).The renal sparing effect of Carvedilol plays a vital role in choosing this very own drug as antihypertensive for the elderly. It reduces the mean arterial pressure without altering or compromising the renal blood flow and urinary sodium excretion. Many studies revealed the antioxidant property of Carvedilol on ROS (reactive oxygen species).This study contributes for the nitric oxide scavenging action of Carvedilol 3.125mg.

Vitamin C is a much known potent antioxidant.

Both the drugs are compared with the standard to reveal the percentage of scavenging action of nitric oxide.

Objective

In this study we are intended to find antihypertensive drug Carvedilol (3.125mg) percentage of scavenging action of nitric oxide radicals against the standard ascorbic acid and commercially available vitamin C.

Materials and Methods

Principle:

Sodium nitroprusside in aqueous solution at physiological pH spontaneously generates Nitrite oxide which interacts with oxygen to produce Nitrite ions, which can be measured at 550nm by spectrophotometer in the presence of Griess reagent (Kumar S *et al*., 2008).

Nitric Oxide Scavenging Activity:

1. Test sample: crude drug of Carvedilol (3.125mg)
2. Reference antioxidant: Ascorbic acid
3. Solvent: sodium nitroprusside in phosphate buffer
4. Reagent: Griess reagent
5. Spectrophotometer

Procedure:

The crude drug extracts (Tablet. Carvedilol 3.125mg and commercially available vitamin C) was dissolved in distilled water (separately) for this quantification. Sodium Nitroprusside (5mM) in standard phosphate buffer saline (0.025M, pH 7.4) which was incubated with 100 mg/ml of sample and tubes were incubated at 29°C for 3 hours. Control experiment without the test compounds but with equivalent amount of buffer was conducted in an identical manner. After 3 hours incubated samples were diluted with 1 ml of Griess reagent. The absorbance of the colour developed during diazotization of Nitrite with sulphanilamide and its subsequent coupling with Napthyl ethylene diamine hydrochloride was observed at 550nm on spectrophotometer. Same procedure was done with ascorbic acid which was standard in comparison to sample.

Calculations

$$\text{Inhibition (\%)} = \frac{\text{(Control - test) x 100}}{\text{Control}}$$

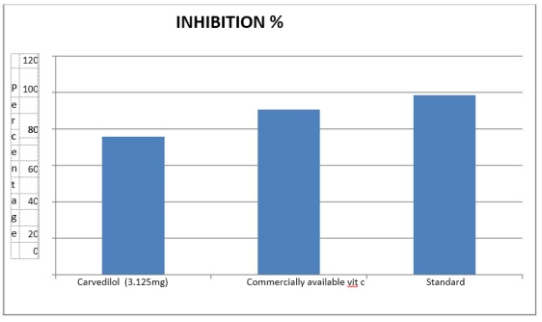
RESULTS

Table 1: Comparison of percentage of inhibition of Carvedilol 3.125mg and commercially available Vitamin C with Ascorbic acid (standard)

S.NO.	NAME OF THE SAMPLE	INHIBITION %
1.	Carvedilol (3.125mg)	75.74
2.	Commercial available Vit C	90.58

3	Ascorbic acid (Standard)	98.5

Figure 1: Bar Chart Comparing Percentage of Inhibition of Carvedilol 3.125 mg and commercially available vitamin C with Ascorbic Acid (standard)



DISCUSSION

The nitrogen oxide scavenging activity was recorded in terms of percentage Inhibition. It was observed from that both Carvedilol 3.125 (75.74%) and commercially available Vitamin C (90.58%) has shown nitrogen oxide scavenging activity (Table 1). The Results obtained were comparative to Ascorbic acid standard. Higher Percentage Inhibition indicates better scavenging activity or antioxidant potential. When compared to commercially available vitamin c and standard Carvedilol 3.125mg shows an appreciable efficacy in inhibiting oxidative stress. (Figure.).

Apart from its antihypertensive action Carvedilol 3.125 possess scavenging action of free radicals thereby reducing oxidative stress and improves the prognosis of co morbid conditions in a hypertensive.

CONCLUSION

In this study antihypertensive Carvedilol 3.125 has additional antioxidant activity which makes it a novel therapy for the management of Hypertension.

LIMITATIONS

This study was done with lower dose of Carvedilol, the amount of antioxidant property in higher doses can be further assessed also other methods of evaluation of antioxidant can also be done both in vivo and in vitro studies.

ACKNOWLEDGEMENT

I sincerely thank my peers, colleagues, professors, college (SBMCH) and laboratory for helping me to bring out this study.

REFERENCES

1. Lawes CM, Vander HS, Rodgers A. Global burden of blood pressure related disease,2001.Lancet.2008;371:1513-8.
2. EganBM,ZhaoY,Axon RN.US trends in prevalence ,awareness, treatment, and control of hypertension,1988-2008,JAMA.2010;303:2043-50.
3. Ruffolo RR Jr et al ;The pharmacology of Carvedilol,Eur J Clin Pharmacol 1990;38 Suppl 2:s 82-8
4. Ana M .Briones et al(2010);Oxidative stress and Hypertension :Current concepts ;Curr Hypertens Rep(2010)12:135-42
5. Miller, H.E., Rigelhof, F., Marquart, L., Prakash, A., and Kanter, M. (2000) Cereal Foods World 45(2), 59-63.
6. Miller, H.E., Rigelhof, F., Marquart, L., Prakash, A., and Kanter, M. (2000) J. Am. Coll. Nutr. 19(3), 312S-319S.
7. Prior, R.L., Cao, G., Martin, A., Sofic, E., McEwen, J.,O'Brien, C., Lischner, N., Ehlenfeldt, M., Kalt, W., Krewer,G., & Mainland, C.M., (1998) J. Agric. Food Chem. 46,2686-2693.
8. Cao, G., Verdon, C.P., Wu, A.H.B., Wang, H., & Prior,R.L. (1995) Clin, Chem., 41, 1738-1744.
9. Vinson, J.A., Hao, Y., Su, X., & Zubik, L. (1998) J. Agri.Food Chem. 46, 3630-3634.
10. Reactive Species and Antioxidants. Redox Biology Is a Fundamental Theme of Aerobic Life. Halliwell, Barry. 2, Singapore : s.n., June 2006, Plant Physiology : American Society of Plant Biologists, Vol. 141, pp. 312-322.
11. Oxidative Stress and Neurodegenerative Diseases: A Review of Upstream and Downstream Antioxidant Therapeutic Options. Bayani Uttara, Ajay V. Singh, Paolo Zamboni. 1, Jalgaon : s.n., March 2009, Currrent Neuropharmacology, Vol. 7, pp. 65-74.
12. Marcocci, I., Marguire, J.J., Droy-lefaiz, M.T., Packer, L., 1994. The nitric oxide scavenging properties of Ginkgo biloba extract. Biochem. Biophys. Res. Commun. 201, 748–755.
13. Marletta, M.A., 1989. Nitric oxide: biosynthesis and biological significance. Trends Biochem. Sci. 14 (12), 488–492.
14. McCord, J., Fridovich, I., 1969. Superoxide dismutase, an enzymic function for erythrocuprin. J. Biol. Chem. 244, 6049–6055.
15. Moncada, S., Palmer Jr, R.M., Higgs, E.A., 1989. Biosynthesis of nitric oxide from L-arginine: a pathway for the regulation of cellfunction and communication. Biochem. Pharmacol. 38, 1709–1715.
16. Meyer, A.S., Isaksen, A., 1995. Application of enzymes as food antioxidants. Trends Food Sci. Technol. 6, 300–304. Azar Baradaran, Hamid Nasri et al; Oxidative stress and hypertension: Possibility of hypertension therapy with antioxidants; J Res Med Sci.2014 Apr,19(4):358-367.
17. Hyunyun Kim et al;Therapeutic strategies for oxidative stree related cardiovascular diseases: Removal of excess reactive oxygen species in adult stem cell:Oxidative Medicine and Cellular Longetivity Volume 2016 article ID:2483163,11
18. Thomas E.Andreoli: Free radicals and oxidative stress; The American Journal of medicine ,August 16,2004
19. Fogliano, V., Verde, V., Randazzo, G., Ritieni, A., 1999. Method for measuring antioxidant activity and its application to monitoring antioxidant capacity of wines. J. Agric. Food Chem. 47, 1035–1040.
20. Frei, B., Stocker, R., England, L., Ames, B.N., 1990. Ascorbate the most effective antioxidant in human blood plasma. Adv. Med. Exp. Biol. 264, 155–163.
21. PÁL PACHER, JOSEPH S. BECKMAN, and LUCAS LIAUDET Nitric Oxide and Peroxynitrite in Health and Disease:Physiol Rev. 2007 Jan; 87(1): 315–424.