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Antioxidant Activity and Free Radical Scavenging Properties of Captopril

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Several diseases are associated with oxidative stress caused by free radicals and reactive oxygen species. In this study, antioxidant activity of captopril was studied using *in vitro* assays systems. Free radical scavenging and reducing power were determined with diphenyl picryl hydrazyl free radical (DPPH method) and potassium ferricyanide method, respectively. The results of this study showed that captopril possessed a significant free radical scavenging and reducing power properties and there were a clear correlation exists between antioxidant activity and concentration of captopril. Percentage of free radical scavenging of captopril was more than 92 % at concentration 0.08 mM.

Key Words: Captopril, Oxidative stress, Free radical scavenging, Reducing power.

INTRODUCTION

Active oxygen and free radicals, such as hydroxyl radical and hydrogen peroxide are produced in the human body by normal metabolic action. The human is equipped with defense systems, including antioxidant compounds and enzymes which detoxified these reactive oxygen species (ROS). Unfortunately, the increasing level of these ROS can lead to cell injury, death and following to chronic diseases such as cancer and atherosclerosis[1,2]. Free radicals that have one or more unpaired electrons are produced during normal and pathological cell metabolism. Reactive oxygen species (ROS) react easily with free radicals so that they will be changed to their radical forms. Reactive oxygen species are various forms of activated oxygen, which include free radicals such as superoxide anion radicals ($O_2^{\bullet -}$) and hydroxyl radicals ($OH^{\bullet}$), as well as non-free radical species (H_2O_2)[3]. Antioxidants provide protective effects for organism againts damage induced by uncontrolled production of ROS. So they could protect macromolecules and organelles against toxicity induced by oxidative stress[4].

Although a number of natural and synthetic antioxidant have already been known, the search for more effective and less toxic antioxidants is continued. Captopril, an angiotension-converting enzyme inhibitor (Fig. 1) is widely used in the treatment of hypertension. Results of an *in vivo* study conducted by Chopra *et al.*[5], confirmed antioxidant properties of captopril, probably related to presence of unblocked sulfhydryl group (SH). Some other experimental studies[5-7] have suggested that captopril may exert some beneficial effects in the clinical setting as a result of its thiol group-related antioxidant properties. In this regards, captoperil has been shown to scavenge efficiently only hydroxyl radical ($OH^{\bullet}$) and hypochlorous acid ($HOCl^{\bullet}$)[5]. However, the results of the antioxidant properties of captopril are controversial. For example, in a study conducted by Lapenna[8] captopril was incapable of enhancing antioxidant properties of human plasma, of protecting it against specific oxidative attact and of decreasing systemic oxidant load *in vivo*.

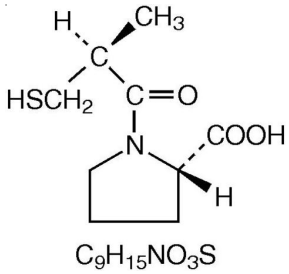

Fig. 1. Chemical structure of captopril

Therefore, the present study was designed to investigate the free radical scavenging property and reducing power potency of captopril with *in vitro* assay systems.

EXPERIMENTAL

Captopril was provided by Daru Paksh (Pharmaceutical Company, Iran). Stable 1,1-diphenyl-2-picryl hydrazyl radical (DPPH) was from Sigma and Fluka chemical Co. (Buchs, Switzerland), respectively. Other chemicals were obtained from commercial companies. A digital double beam spectrophotometer (Perkin-Elmer EZ201, USA) was used for conventional

measurements. All pH measurements were done with a digital pH meter model Metrohm 744 (Switzerland).

Measurement of free radical scavenging activity: The free radical-scavenging capacity of captopril was determined as bleaching of the stable 1,1-diphenyl-2-picryl hydrazyl radical (DPPH)[9]. The different concentrations of captopril (0.025-0.2 mM) were added, at an equal volume, to ethanolic solution of DPPH (100 mM). After 15 min at room temperature, the absorbance was recorded at 517 nm. The experiment was performed in triplicate. Ascorbic acid was used as an antioxidant standard. Per cent of scavenging was calculated using the formula $\left[\frac{(\text{Control}-\text{Test})}{\text{Control}}\right]\times 100$.

Reducing power activity: Captopril was added to potassium ferricyanide [$K_3Fe(CN)_6$] (1 mL, 1 %) at different concentrations (0.025-0.5 mM in PBS, pH 7.4). The mixture was incubated at 50 ºC for 20 min at bath water. For stopping reaction, tricholoroacetic acid (10 %) was added to the mixture and then 1 mL of $FeCl_3$ (0.1 %) was added to this solution. Absorbance was measured at 700 nm. Per cent of reducing power was calculated using the formula $\left[\frac{(\text{Test}-\text{Control})}{\text{Test}}\right]\times 100$. Acid ascorbic was used as a standard.

Statistical analysis: Data were analyzed with Excel software. The data are presented as means ± SD. All measurements were performed at triplicates.

RESULTS AND DISCUSSION

Captopril showed an excellent free radical inhibition at concentration dependent manner with similar to ascorbic acid as a well known antioxidant. The maximum free radical scavenging properties were at 92.8 and 93.1 % for captopril and acid ascorbic, respectively, at 0.08 mM (Fig. 2). The scavenging effects of ascorbic acid as an antioxidant standard were similar to the captopril showed high antioxidant activity of it. In addition, captopril exhibited high reducing power activity. The per cent of reducing power activity was about 83 and 87 % at the concentration of 0.5 mM for captopril and ascorbic acid, respectively (Fig. 3). The present study was carried out to evaluate free radical scavenging and reducing power activity of captopril. Determination of scavenging activity of the stable DPPH radical is a widely used method to evaluate the free radical-scavenging ability of various samples[10]. DPPH is a stable, nitrogen-centered free radical, which changes from violet to yellow upon reduction by the process of hydrogen or electron donation. Substances that can perform this reaction are considered antioxidants and therefore radical scavengers[11]. The reduction capability of DPPH radical in the current study was determined by the decrease in its absorbance at 517 nm, which is induced by different antioxidants. Captopril showed potent radical scavenging properties using the DPPH method similar to the ascorbic acid as a standard antioxidant.

Reducing power determination[12] is based on the principle that substances with reduction potency, react with potassium ferricyanide (Fe^{3+}) to form potassium ferrocyanide (Fe^{2+}),

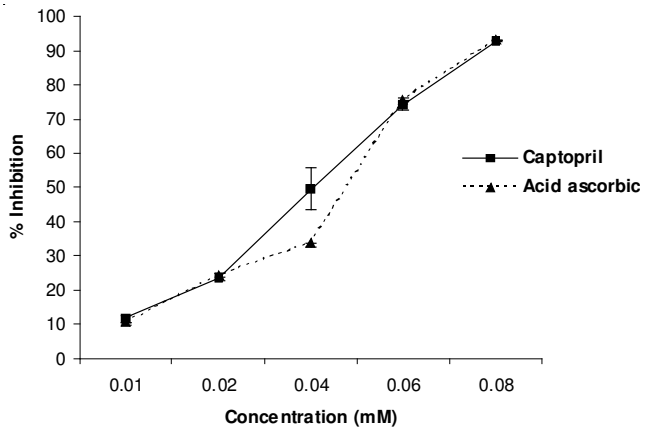

Fig. 2. Scavenging effect of different concentration of captopril and acid ascorbic on the 1,1-diphenyl-2-picrylhydrazyl (DPPH) free radical at 517 nm

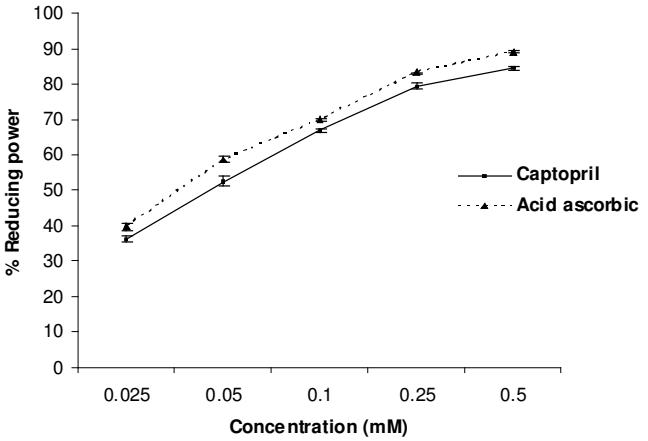

Fig. 3. Percentage of reducing power of captopril on potassium ferricyanide. Ascorbic acid was used as positive standard

which then reacts with ferric chloride to form ferric ferrous complex that has an absorption maximum at 700 nm. Reductones are believed not only to react directly with peroxides but also prevent peroxide formation by reacting with certain precursors[13]. The reducing power of the captopril increases with the increase in amount of captopril (Fig. 3).

Captopril (Fig. 1), an inhibitor of angiotensin converting enzyme (ACE), has also potential protective effects, including protection against lead toxicity[14], erythrocytes damage[15], radiation and chemical hazardous[16,17]. In these studies, captopril had significant antioxidant properties with increasing *in vivo* enzymes and non-enzymes defense system, such as superoxide dismutase and glutathione[14,18].

One thiol-containing molecule of captopril can donate one electron, thereby quenching one free radical. Furthermore, since captopril dissolved in ethanol and PBS retaining antioxidant power, captopril could augment lipophilic and hydrophilic antioxidant defense[19]. However, captopril can form complex with metal that inhibited the superoxide-mediated reduction and oxidative stress[20].

Conclusion

It is well known that free radicals are one of the causes of several diseases. The results from the two *in vitro* antioxidant assay systems revealed that captopril had significant antioxidant

activity. Captopril has an excellent free radical scavenging effect and reducing potency so that this antioxidative effect can participate in beneficial property of captopril along with its therapeutic effects in heart and vascular diseases.

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