

The Effect of Some Phenol Derivatives as Antileukemic Agents on Lipid Peroxidation

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Key Wards: Phenol derivatives, anthileukemic agents, ALL, AML, CLL, CML and peroxyntirite. 1

Summary:

Background:-

The production of reactive oxygen species in most diseases including leukemia (type of cancer) is confirmed to be the most destructive process to human cell.

Objective:-

Potent antioxidant is needed to overcome the lipid peroxidation and oxidative stress. Polyphenolic compounds are group of naturally occurring compounds in different plants. They are promising product to protect, and prevent leukemia and many types of cancer by different mechanisms.

Result:

The effect of polyphenolic compounds (ellagic and tannic acid) on peroxyntirite was investigated in different types of leukemia (AML, ALL, CML and CLL). The results revealed the effectiveness of ellagic acid(EA) and tannic acid (TA) in treatment of leukemia in

vitro study, and the peroxynitrite concentration was reduced to normal value. The results showed that EA was most potent than TA.

Introduction:

Leukemia⁽¹⁾ is a group of malignant disorders of the haemopoietic tissue characterized by the accumulation of abnormal white cells in the bone marrow. These abnormal cells may cause bone marrow failure, a raised circulating white cell count and infiltrate other organs.

According to the French-American British (FAB) system leukemia classified into acute and chronic type. Acute leukemia is divided into acute myeloblastic (AML) and acute lymphoblastic leukemia (ALL) and other subdivided.

Chronic leukemia also is divided into chronic myeloblastic leukemia (CML) and chronic lymphoblaste leukemia (CLL).

Free radical system has been suggested and described to be implicated in the pathogenesis of many diseases such as cardiovascular disease, some forms of cancer, cataract and related macular degeneration⁽²⁻⁵⁾.

Nitric oxide is known to react with superoxide anion (produced under condition of oxidative stress) yielding the powerful oxidant, peroxynitrite (ONOO) that may alter vascular function⁽⁶⁾.

Peroxyntirite is one of the most potent oxidizing agent with pronounced deleterious effects through oxidation of a number of biomolecules including membrane phospholipids, thiol deoxyribose and through inhibition of mitochondrial electron transport⁽⁷⁻⁹⁾. Therefore peroxynitrite should be scavenged by antioxidant molecules when it generated.

The plant is rich source of poly phenolic compound which has been recognized for many years as an antibacterial, antifungal and antioxidant agents⁽¹⁰⁾.

More investigations were carried out related to the role of some dietary polyphenolic i.e ellagic acid (EA), tannic acid (TA), caffiec

acid (CA) and ferulic acid (FA), which conducted in inhibition of promotion phase of carcinogenesis⁽¹¹⁾. Ellagic acid, which has an important antioxidant potential, plays a great role on human health to protect against reactive oxygen species⁽¹²⁾.

Tannic acid might be valuable in cancer therapy and/ or prevention⁽¹³⁾ and may be effective not only against tumor initiation and complete carcinogenesis but also against the promotion phase of tumorigenesis⁽¹⁴⁾.

Subjects and method:

Selection of subjects:-

Blood samples were collected from a ninety leukemia patients with age range 18-68 years at the Medical City Hospital in Baghdad. Seventy five healthy individual were selected with age range 18-40 years.

Determination of peroxynitrite concentration according to the Vanuffelen et. al.; (1998) method⁽¹⁵⁾ before and after addition of EA and TA as treatment.

Result and Discussion:

Lipid peroxidation products measured as (ONOO) content were detectable in a significant higher levels in all types of leukemia compared to the normal control, as shown in figures (1) and (2).

The high level of peroxynitrite in serum of AML patients compared with control and all types of leukemia could be due to the greater damage in the tissue. Some studies have been show that many diseases including certain types of cancer (i.e lung, liver, breast, skin and colon) are the direct results of free radical damage in the body^(16,17).

In the present study the effect of some poly phenolic compounds (i.e EA and TA) were investigated in vitro by the addition of different concentrations of EA and TA to human serum taken from patients with different types of leukemia.

The concentration of (EA and TA) was chosen to be 10 μM among other concentrations studied for its effectiveness⁽¹⁸⁾.

The addition of 10 μM of EA and TA to the sera of patients with leukemia reduce peroxy nitrite levels. This is in a good agreement with other^(19,21).

Poly phenolic compounds inhibits lipid peroxidation and prevent different diseases caused by free radicals^(22,23).

The present study showed that EA was the most potent polyphenol chemopreventive agents than TA as shown in fig.(1) and (2), the results are in agreement with other researches^(24,25).

The diversity in structure and reactivity between different poly phenolic compounds is principally due to variation in the patterns of hydroxylation and methylation of the aromatic rings⁽²⁶⁾, EA acts as a scavenger to bind and inactivate cancer causing chemicals⁽²⁷⁾.

Some researches emphasize the action of EA as an anticarcinogenic agents, which has been shown to inhibit chemically induced cancer in the lung, liver, skin and blood^(28, 29).

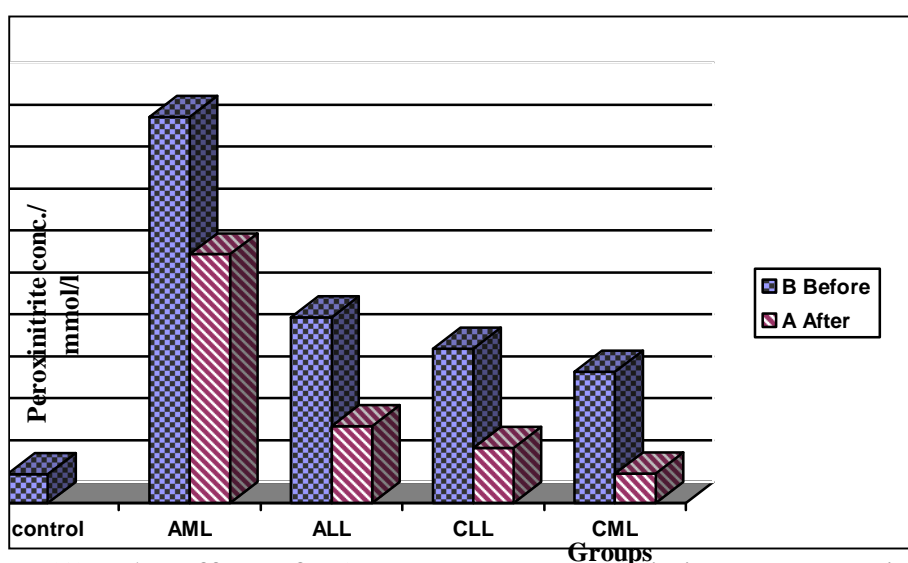


Figure (1): The effect of EA on serum peroxy nitrite concentration in all patient groups and normal control group.

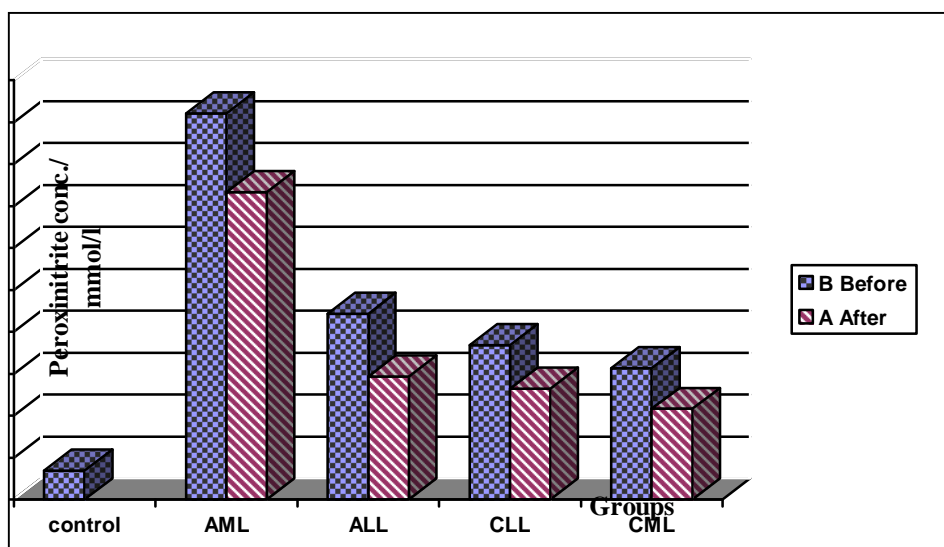


Figure (2): The effect of TA on serum peroxy nitrite concentration in all patient groups and normal control group.

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