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The Effect of Some Polyphenolic compounds on Serum Peroxynitrite of Leukemics

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Abstract:

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.

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.

The effect of polyphenolic compounds (ellagic and tannic acid) on peroxynitrite was investigated on ninety patients with different types of leukemia (AML, ALL, CML and CLL), and seventy five healthy individuals as control group. The age of all studied groups range from (18-40) years. The results revealed the effectiveness of ellagic acid (EA) and tannic acid (TA) in lowering peroxynitrite levels in sera of leukemic patients *in vitro* study, which the peroxynitrite concentration was reduced to normal value. The results showed that EA was most potent than TA.

Introduction:

Leukemia 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[(1)].

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 super oxide anion (produced under condition of oxidative stress) yielding the powerful oxidant, peroxynitrite ($ONOO^-$) that may alter vascular function [6, 7].

Peroxyinitrite is one of the most potent oxidizing agent with pronounced deleterious effects through oxidation of a number of bimolecular including membrane phospholipids, thiol deoxyribose and through inhibition of mitochondrial electron transport .Therefore peroxynitrite should be scavenged by antioxidant molecules when it generated [8-10].

The plants are rich sources of polyphenolic compound which has been recognized for many years as an antibacterial, antifungal and antioxidant agents[11]. 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 postulated for inhibition of promotion phase of carcinogenesis[12]. Ellagic acid, which has an important antioxidant potential, plays a great role on human health to protect against reactive oxygen species which acts as free radical scavenger [13].

Tannic acid might be valuable in cancer therapy and/ or prevention and may be effective not only against tumor initiation and complete carcinogenesis but also against the promotion phase of tumorgensis [14 ,15].

Subjects and method:

Selection of subjects:-

Six ml of blood were collected from ninety leukemic patients at the Medical City Hospital in Baghdad, in addition to seventy five healthy individual as control group. The age of all studied group range from(18-40) years.The blood were transferred into disposable tube and centrifuged (750xg,10 min) within 15 min after collection.The produced serum stored at -20 C^0 until used.The concentration of peroxynitrite was determined in serum according to the Vanuffelen method[16] before and after addition of EA and TA.

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 table (1).

Table (1): Levels of peroxynitrite concentrations in sera of control and leukemic patients groups before(B) and after addition of ellagic acid (EA)and tannic acid (TA).

Subjects	No.	Peroxynitrite	Conc. (m	mol/l)	t-Test
		B	EA	TA	
Control	75	0.138 ±0.01	----------	----------	P<0.05
AML	20	1.843±0.90	1.186±0.50	1.399±0.52	P<0.05
ALL	20	0.887±0.07	0.368±0.03	0.520±0.03	P<0.05
CLL	25	0.738±0.06	0.263±0.02	0.451±0.029	P<0.05
CML	25	0.627±0.04	0.141±0.01	0.370±0.02	P<0.05

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 [(5)].

In the present study the effect of some polyphenolic compounds (i.e. EA and TA) were investigated *in vitro* .The concentration of (EA and TA) was chosen to be 10 μM among other concentrations studied for its effectiveness [(17)].

The additions of 10 μM of EA and TA to the sera of patients with leukemia reduce peroxynitrite levels as shown in figures (1&2) respectively.The results are in agreement with other studies[(5,10,18)].

The present study showed that EA was the more potent than TAwhich could be recommended as chemopreventive agent.

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 [(19,20)].

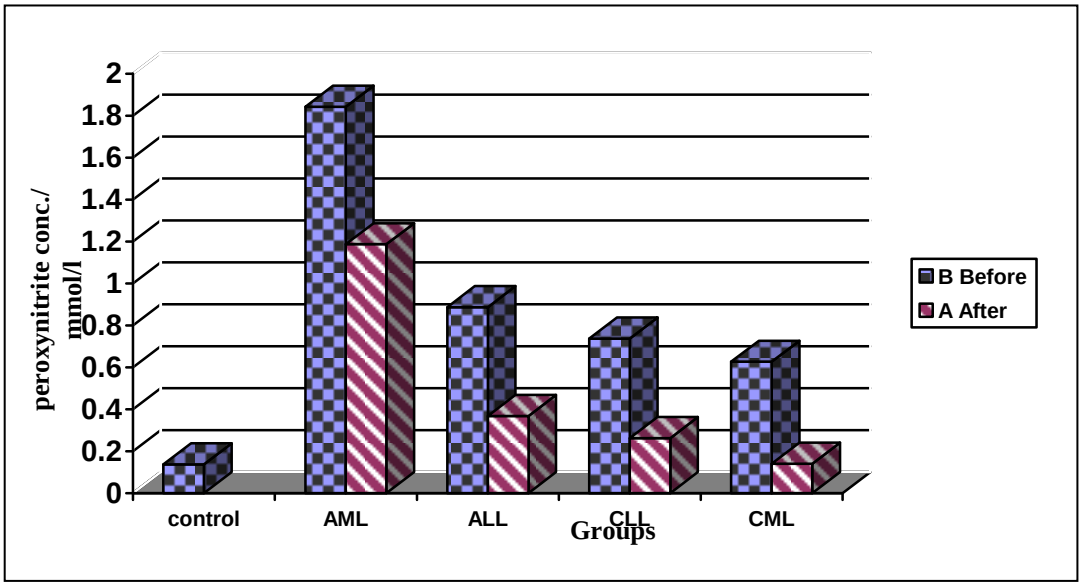

Figure (1): The effect of EA on serum peroxynitrite concentration in all patient groups and normal control group.

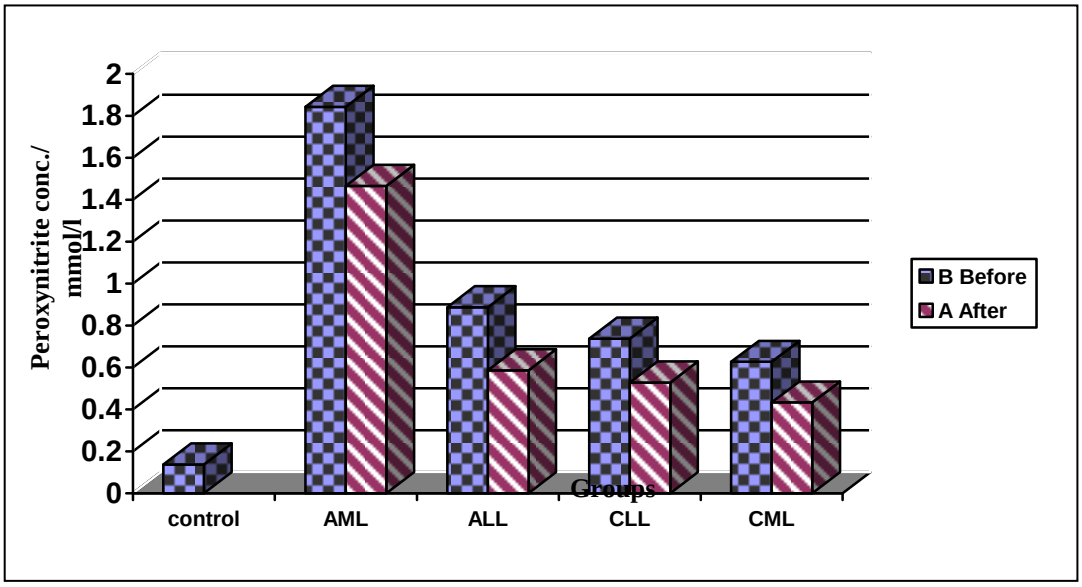

Figure (2): The effect of TA on serum peroxynitrite concentration in all patient groups and normal control group.

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تأثير بعض مركبات متعدد الفينول على مستوى البيروكسي نايترايت في امصال مرضى ابيضاض الدم

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الخلاصة:

أن أنتاج أصناف الأوكسجين الفعالة في معظم الإمراض ومن ضمنها ابيضاض الدم (نوع من السرطان) يعتبر أساس لتحطيم خلايا الإنسان.بالتالي كانت الحاجة الى مضادات الأكسدة القوية مهمة لإزالة الأكسدة الفوقية للدهون والشد ألتأكسدي . مركبات متعدد الفينول موجودة في معظم النباتات ،وهي تعمل على حماية ومنع ابيضاض الدم وأنواع أخرى من السرطان بواسطة ميكانيكيات مختلفة .

أجريت الدراسة على 90 مريضاً مصاباً بابيضاض الدم مع 75 شخصاً طبيعياً كمجموعة سيطرة.تتراوح أعمار المجاميع المدروسة بين (18–40)سنة .

تم دراسة تأثير مركبات متعدد الفينول (حامض اللاجيك وحامض التانيك) على البيروكسي نايتريت في أنواع مختلفة من سرطان ابيضاض الدم (AML,ALL,CM,CLL) في دراسة خارج جسم الكائن الحي.

بينت النتائج فعالية حامض اللاجيك وحامض التانيك حيث انخفض تركيز البيروكسي نايتريت إلى القيم الطبيعية .كما بينت النتائج ان حامض اللاجيك اقوى تاثير من حامض التانيك.