Original Article

Effect of Some Polyphenolic Compounds on Biochemical Parameters in Leukemic Patients

Wafa F. Al-Taie* **PhD**
Kismat M. Turki** **PhD**
Zeinab M. AL-Rubaie* **PhD**

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Abstract:

ackground : Polyphenolic compounds are groups of naturally occurring compounds in different plants. They are promising product to protect, and prevent leukemia and many types of cancer by different mechanisms.
Objectives: The present study designed to study the effect of polyphenolic compounds [Ellagic acid (EA), Tannic acid (TA) and Caffiec acid (CA)] on GOT,GPT activities and total protein TP concentration in all types of leukemia [acute myeloblastic leukemia (AML), acute lymphoblastic leukemia (ALL), chronic myeloblasti leukemia (CML) and chronic lymphoblastic leukemia (CLL)],in addition to compare the potency of these compounds among each other.
Patients and Methods: Blood samples were collected from a hundred leukemic patients. In addition fifty healthy subjects age matched were chosen as control group. Transaminases (GOT and GPT) activities and total protein concentration in sera of all studied groups were determined before and after addition of 10 mM (EA, TA and CA)
Results: There is a significant increase in serum GOT,GPT activity and TP concentration for all leukemic groups compared to control. The elevated values of GOT, GPT activities and TP concentration in patients were returned to about normal values in most cases after addition of 10 mM (EA, TA and CA).
Conclusion: Results showed the effectiveness of polyphenolic compounds (EA, TA and CA) in treatment of leukemia in vitro study , also, results revealed that EA was the most potent compound among the types of polyphenolic compounds studied in affecting the parameters to be close to normal values.
Key words: polyphenolic compound, leukemia , GOT ,GPT

Introduction:

Leukemia, in common with most other cancers, is monoclonal. A broad classification includes two large groups historically designated acute and chronic. The two major groups of acute leukemia are myeloblastic leukemia (AML) and lymphoblastic leukemia (ALL). Chronic leukemia also divided into two main groups; chronic myeloid leukemia (CML), and chronic lymphoblastic leukemia (CLL) (1). Flavonoids are large groups of polyphenolic antioxidant that occur in several fruits, vegetables, and beverages (2). The plants are rich source of polyphenols which have been recognized for many years as an antibacterial and antifungal agents, but only more recently as an antitumor compounds(3). Recent researches emphasize the action of some polyphenols as anticarcinogenic agents,which have been shown to inhibit cancer in the lung, liver, skin, esophageus, and blood (4). Transaminases (GOT and GPT) catalyze reactions called transaminations. All transaminases have prosthetic group, pyridoxal phosphate (PLP) as an intermediate carrier of amino group (5). Measurement of GOT and GPT activities in blood serum is important in some medical diagnoses(6).The major diagnostic application used GOT activities are the investigation of myocardial infarction, liver disease and muscle disease. Therefore, elevations in aminotransferases signify pathology (7). Thus, present study designed to study the effect of polyphenolic compounds on GOT, GPT activities and TP concentration in all types of leukemia, and to compare the potency of these compounds among each other.

* *Dept. of Chemistry Ibn-AlHaitham /College of Education/University of Baghdad*
** *Dept. of Physiological Chemistry/ College of Medicine /University of Baghdad*
Email: Alizeinabah@yahoo.com

Patients and Methods:

Blood samples were collected from a hundred leukemic patients ,that 25 patients diagnosed with (AML) and 25 patients diagnosed with (ALL),25 patients diagnosed with (CML), and 25 patients diagnosed with (CLL). In addition to fifty healthy subjects age matched were chosen as control group. Determination of transaminases (GOT and GPT) activities in sera of all studied groups was performed by colorimetric method of Reitman and Frankel (8). Determination of total serum protein concentration was carried out according to Lowry's method (9) using bovine serum albumin (BSA) as a standard protein. (GOT and GPT) activities and total protein concentration in sera of all studied groups were determined before and after addition of 10 mM (EA, TA and CA).

Results:

As shown in tables (1A, 1B, 1C) there is a significant increase in serum GOT, GPT activities for all leukemic groups compared to control group. There is also a significant increase in serum GPT activities for all patients groups compared to control as shown in tables (2A, 2B, 2C).After the addition of 10 mM of (EA, CA and TA) to the sera of leukemia patients, the activities of both GOT and GPT were reduced significantly.

Table (1A): The effect of EA on serum GOT activity in all patient groups and normal control before (B) and after (A) addition of EA.

Type	GOT activity U/L mean ± SD		T-Test
	B	A	
Control	15.86±4.06	-	P<0.05
AML	63.66±10.41	41.66±10.00	P<0.05
ALL	36.06±3.05	16.37±2.34	P<0.05
CML	34.55±5.99	19.75±3.74	P<0.05
CLL	34.72±6.73	18.44±5.81	P<0.05

Table (1B): The effect of CA on serum GOT activity in all patient groups and normal control before (B) and after (A) addition of CA.

Type	GOT activity U/L mean ± SD		T-Test
	B	A	
Control	15.86±4.06	-	P<0.05
AML	48.50±2.59	43.12±3.69	P<0.05
ALL	37.37±4.96	31.25±5.31	P<0.05
CML	27.68±5.99	22.50±3.74	P<0.05
CLL	35.66±6.73	29.75±5.81	P<0.05

Table (1C): The effect of TA on serum GOT activity in all patient groups and normal control before (B) and after (A) addition of TA.

Type	GOT activity U/L mean ± SD		T-Test
	B	A	
Control	15.86±4.06	-	P<0.05
AML	46.38±4.40	31.80±4.20	P<0.05
ALL	34.22±4.42	20.88±4.53	P<0.05
CML	32.61±3.83	20.44±1.50	P<0.05
CLL	28.62±5.48	17.81±2.40	P<0.05

Table (2A): The effect of EA on serum GPT activity in all patient groups and normal control before (B) and after (A) addition of EA.

Type	GPT activity U/L mean ± SD		T-Test
	B	A	
Control	12.96±4.22	-	P<0.05
AML	46.00±4.57	30.83±4.50	P<0.05
ALL	34.87±3.04	19.18±1.66	P<0.05
CML	29.77±2.86	17.55±2.22	P<0.05
CLL	33.05±4.02	21.55±3.88	P<0.05

Table (2B):The effect of CA on serum GPT activity in all patient groups and normal control before (B) and after (A)addition of CA.

Type	GPT activity U/L mean ± SD		T-Test
	B	A	
Control	12.96±4.22	-	P<0.05
AML	47.93±2.74	41.06±2.54	P<0.05
ALL	32.00±4.26	26.12±5.20	P<0.05
CML	30.62±2.70	24.35±3.33	P<0.05
CLL	26.05±2.00	20.66±2.04	P<0.05

Table (2C): The effect of TA on serum GPT activity in all patient groups and normal control before (B) and after (A) addition of TA.

Type	GPT activity U/L mean ± SD		T-Test
	B	A	
Control	12.96±4.22	-	P<0.05
AML	45.66±5.66	33.55±5.74	P<0.05
ALL	34.77±7.35	23.22±6.24	P<0.05
CML	31.05±4.70	20.66±3.47	P<0.05
CLL	27.50±2.63	18.12±2.57	P<0.05

Total protein concentration in serum

The mean (± SD) values of serum total protein concentration in control and all types of leukemia before and after addition of (EA, CA, TA) are shown in tables 3A,3B,and 3C.There were significant elevation in levels of TP concentration in all types of leukemia compared with control group. After the addition of 10 µM of (EA, CA, TA) the TP concentration were decreased to about the normal values

Table (3A): The effect of EA on TP concentration in all patient groups and normal control before (B) and after (A)addition of EA.

Type	TP concentration g/L mean ± SD		T-Test
	B	A	
Control	72.86±6.49	-	P<0.05
AML	100.00±8.41	67.77±2.48	P<0.05
ALL	100.11±10.82	67.33±3.46	P<0.05
CML	88.22±6.39	71.00±6.22	P<0.05
CLL	90.37±3.73	69.12±6.12	P<0.05

Table (3B): The effect of CA on TP concentration in all patient groups and normal control before (B) and after (A)addition of CA.

Type	TP concentration g/L mean ± SD		T-Test
	B	A	
Control	72.86±6.49	-	P<0.05
AML	102.37±6.75	90.87±6.15	P<0.05
ALL	99.62±10.50	89.25±8.64	P<0.05
CML	90.62±3.24	80.25±5.06	P<0.05
CLL	88.16±3.65	79.83±3.31	P<0.05

Table (3C): The effect of TA on TP concentration in all patient groups and normal control before (B) and after (A)addition of TA.

Type	TP concentration g/L mean ± SD		T-Test
	B	A	
Control	72.86±6.49	-	P<0.05
AML	101.33±6.83	75.66±3.46	P<0.05
ALL	93.75±4.86	77.75±3.53	P<0.05
CML	88.55±6.63	70.66±3.39	P<0.05
CLL	91.33±4.06	71.77±4.43	P<0.05

Discussion:

The elevation in GOT and GPT activities either reflecting extensive liver damage, or elevated expression of the enzyme in leukemic patients (10). Results indicated that polyphenols compounds are commonly used hepatoprotective agent. The effect of each active component of *in vitro* evaluation of walnut polyphenols on CCl4-induced cytotoxicity in primary cultured rat hepatocytes walnut polyphenols is believed to be the most important active compound responsible for hepatoprotective effect. The results are in agreement with other researches (11-13). The liver is known to be a key organ in the metabolism and detoxification, is vulnerable to damage induced by a huge

variety of chemicals. When the liver cell membrane is damaged, a variety of enzymes normally located in the cytosol are released into blood stream. The same author, Hiroshi et al. (2006) reported that 50% EtOH extract from endocarps of walnuts on mice liver injury models induced by carbon tetrachloride at the dose of 100 and 200 mg/kg significantly suppressed GOT and GPT deviations. Polyphenolic compounds were found to be principal constituents with hepatoprotective activity against oxidative damage (14). The elevation in TP concentration could be due to the presence of paraprotein and Benjones protein which are common in malignant disease (15). Microarray analysis revealed that EA modulates several genes, specifically, over expresses genes involved in DNA repair, such as xeroderma pigmentosum group A complementing protein, DNA ligase III, and DNA excision repair protein, by threefold to eightfold. Also, EA down regulates mitogen-activated protein kinase and MAP kinase , which are involved in key cell-signaling pathways EA as a chemopreventive agent inhibits carcinogen bioactivation, carcinogen-to-DNA binding, cancer cell growth, and increased protein levels (16-18).). The results showed that EA was the most potent among other polyphenolic compounds, and this could be attributed to versions in the pattern of hydroxylation and methylation of the aromatic rings, which give EA its properties as anticarcinogenic by acting as free-radical scavenger (19). The primary antioxidant mechanism of EA has been attributed to the direct scavenging of free radicals, nitrogen reactive species, and ROS, including hydroxyl radicals, peroxyl radicals, NO2 radicals, and peroxynitrite. Other potential protective mechanisms of EA include shielding of DNA from attack and subsequent mutation by its direct association with this macromolecule, inhibition of ROS production, and chelation of metal ions, such as copper. EA at low doses (1 μM) is substantially effective (nearly ٥٠٪ inhibition) in preventing dopamine/Cu (II)-mediated oxidatively generated DNA damage (٢٠). The conclusion could be drowning from this study that polyphenolic compounds (EA, TA and CA) are effectiveness in treatment of leukemia in vitro study. Also, results revealed that EA was the most potent compound among the polyphenolic compounds studied in affecting the GOT ,GPT activities.

Authors Contribution:

The first author design the study, second author write the study and the third author collect the samples and determined the parameters .

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