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In-vivo Antioxidant Effects of the Orally Administered Paracetamol, Aqueous Extracts of *Saliva triloba, and Origanum syriacum*

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Abstract

The plant extracts are found to be effective against oxidative stress. There are lots of reasons for increased oxidative stress in which environmental factors and life style play a big role. In this study the herbal extracts of *Saliva triloba*, and *Origanum syriacum* used to study antioxidant properties compared to paracetamol. A total of 27 volunteers were divided into 3 groups, 2 groups took 250 ml of aqueous extract of *S. triloba*, and *O. syriacum* for 5 days and 3rd group took paracetamol 500 mg, each tablet twice a day for five days. Blood specimens were collected before taking extract and one hour after taking the first dose at day one and one day after the last dose. Serum Total Antioxidant Status (TAS) and reduced glutathione (GSH), malondialdehyde (MDA) and Superoxide Dismutase (SOD) in RBCs were tested. The oral intake of aqueous extract of the plants for five days increased serum TAS and GSH in RBCs compared to zero time of intake. In addition, oral intake of aqueous extracts of *Saliva triloba* for five days increased significantly, P value ≤ 0.05 the activity of SOD in RBCs as compared to zero time of administration. The herbs extracts of *Saliva triloba* and *Origanum syriacum* have anti-oxidant property compared to paracetamol, so as medicinal herbs with antioxidant effects can inhibit produced oxidative effects.

Keywords: Antioxidant status, Malondialdehyde, Reduced glutathione, Superoxide dismutase

Introduction

There are lots of reasons for increased oxidative stress in which environmental factors and life style play a big role. Antioxidants can stop the harmful consequences of oxidative stress on human health (Valko *et al.*, 2006; 2007).

Medicinal plants are potential sources of natural antioxidants (AS *et al.*, 2020). Natural antioxidants can inhibit the oxidative damages through metal chelating properties and scavenging activity of free radicals (Soobrattee *et al*., 2005); in addition, plant extracts are effective against oxidative stress.

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Salvia triloba and *Origanum syriacum* are the most popular medicinal plants in Lebanon and Jordan that has been commonly used for medical purposes (Barakat & Fatima, 2000).

Saliva triloba, belongs to the Lamiaceae family, commonly referred to as Greek sage, the Arabic Name of *Salvia triloba* is Meramiyyh. It is commonly used to treat gastric disorders, bloating, infections of the mouth, gums, and teeth, stomach discomfort, headaches, common cold, cough, and influenza (Barakat & Fatima, 2000). *Saliva triloba* extracts have anti-inflammatory, antioxidant, antimicrobial and anticancer activities (Kamatou *et al.*, 2005; 2007; 2008; 2010; Añides *et al.*, 2019).

Origanum syriacum L. (Lamiaceae), is often known as white oregano and/or Syrian oregano, and its Arabic name is za'atar (Seidemann, 2005). Previous studies have reported its acetylcholinesterase inhibition and antioxidant activity (Loizzo *et al.*, 2009, Zein *et al.*, 2011); antifungal agent detection (Abou-Jawdah, 2004; Kintzios, 2004); antibacterial activity (Kintzios, 2004; Peña *et al.*, 2019) analgesic activity, expectorant, antirheumatic, sedative, anthelmintic and antiparasitic activities (Zein *et al.*, 2011).

All over the world, paracetamol is an analgesic and antipyretic drug, and single-component and multi-component preparations can be obtained without a doctor's prescription.

In vitro antioxidant properties of *Salvia triloba* and *Origanum syriacum* extracts were previously evaluated (Bilto *et al.*, 2015c). This study proposed to see the antioxidants *in vivo* effects of the orally intake of aqueous extracts of *S. triloba* (leaves), *O. syriacum* (leaves), and Paracetamol.

Materials and Methods

Plant Material

Plant materials: Meramiyyh (leaves), oregano (leaves) were bought from an herbal shop in Madaba city. The herbs are selected according to its wide use as a traditional medicine.

Formation of Aqueous Extracts

250 gram of *S. triloba, O. syriacum* dried and was boiled in 11.250 Liter water for 15 min, and left dousing for 4 hours at 25 °C. Then

the aqueous extract was packed in tidy bottles with a capacity of 1.250 L.

Blood Samples

27 participants were divided into three groups of nine persons, and their demographic data is presented in **Table 1**. The two groups drank 250 ml of water extracts of selected medicinal plants (Meramiyyh, Oregano) 3 for 5 days and the third group took paracetamol (500 mg, each tablet twice a day) for 5 days.

Three blood samples were collected (one before taking water extract, one after 1st dosage taking water extract on day one, and one day after the last dose) in the gel clot activator tube. To separate and collect the serum, the gel tube was centrifuged at 3000 rpm for 10 minutes at 25°C. Then, 2 ml of deionized water was added to the cells in the tube under the gel, the tube was centrifuged at 3000 rpm for 5 min, and the supernatant was collected. For further testing, all specimens were stored at -20 °C.

Table 1. Demographic Data of the Participants

	Age Mean ± S.D.	**Sex (Female/Male)**
O. syriacum	35.8±14.7	4/5
S. triloba	42.8±14.6	6/3
Paracetamol	30.6±9.8	3/6

Serum TAS Assay

TAS analysis of serum was performed using Randox TAS kit. The data is expressed in millimoles/Liter.

MDA Activity in RBC

MDA was measured as a marker of lipid peroxidation using Dormandy's technique (1971) and Thiobarbituric Acid (TBA) with minor modifications. All MDA values were shown in nmol/gHb units.

GSH Activity in RBC

Ellman's technique was slightly modified to analyze red blood cell GSH (Ellman, 1951). All GSH values are expressed in mg/gHb.

SOD Activity in RBC

SOD levels were measured using a Randox kit. The outcomes were displayed as U/gHb.

Statistical Analysis

Mean and standard deviation were analyzed using SPSS software, version.17 to evaluate test data.

Results and Discussion

In vivo study showed that oral intake of *S. triloba* and *O. syriacum* increased serum TAS after 5th day of extract intake. Paracetamol did not affect serum total antioxidant capacity **(Table 2)**.

Oral administration of *S. triloba* and *O. syriacum* also resulted in an increase in GSH in RBCs at 5th day of extract intake. Paracetamol had no effect on GSH in RBCs **(Table 3)**. However, SOD in RBCs increased considerably after five days of oral intake of *S. triloba* extract in comparison to 0 time of intake, whereas, *O. syriacum* and Pracetamol did not increase erythrocyte activity of superoxide dismutase **(Table 4)**.

Saliva triloba, *Origanum syriacum* and Paracetamol did not decrease erythrocyte content of MDA after five days of administration **(Table 5)**.

Table 2. TAS Before and After Oral Intake of the Studied Herbs

	TAS (mmol/l)		
	0 time	1hr (day 1)	Day 6
Saliva triloba	1.12±0.11	1.16±0.15	1.22±0.16*
Origanum syriacum	1.14±0.10	1.21±0.11	1.28±0.09*
Paracetamol	1.4±0.27	1.36±0.3	1.31±0.9

* Each statistic reflects the mean± S.D., (n =9), with a *P value of ≤ 0.05 when in comparison to the 0 time administration.

Table 3. GSH Measured in mg/g Hb Before and After Oral Intake of Studied Herbs

	GSH	
	0 time	**Day 6**
Saliva triloba	0.54±0.09	0.87±0.10*
Origanum syriacum	0.73±0.11	0.80±0.10*
Paracetamol	0.73±0.12	0.75±0.13

***** Each statistic reflects the mean ± standard deviation (n =9), with a *P value of ≤ 0.05 in comparison to the 0 time administration.

Table 4. SOD Measured in U/gHb Before and After Oral Intake of Studied Herbs

	0 time	**Day 6**
Saliva triloba	868.0±167.1	997.5±192.4*
Origanum syriacum	1037.1±155.3	1098.0±181.5
Paracetamol	1114.5±256.6	1091.2±172.1

***** Each statistic reflects the mean± standard deviation (n =8), with a *P value ≤ 0.05 in comparison to the 0 time administration.

Table 5. MDA Measured in nmol//g Hb Before and After Oral Intake of Studied Herbs

	MDA	
	0 time	**Day 6**
Saliva triloba	17.9±3.4	15.8±3.8
Origanum syriacum	17.5±3.4	16.4±3.5
Paracetamol	16.1±3.1	17.8±4.1

* Each number reflects the mean ± standard deviation (n =9).

Oral intake of aqueous extracts of *S. triloba* and *O. syriacum* enhanced the serum TAS after five days of intake. This conclusion is supported with the results of other studies (Bilto & Alabdallat, 2015a; 2015b; Alabdallat, 2016; 2021). Our present study also presented that the plants increased GSH content of RBC after five days of intake. This conclusion is consistent with the results of other studies (Bilto & Alabdallat, 2015a; 2015b; Alabdallat, 2016; 2021) and (El-Dakhakhny *et al.*, 2000; Ali, 2004; Kaleem, *et al*., 2006; EL-shenawy *et al.*, 2008; Asnani & Verma, 2009) who showed that oral treatment of ginger or nigella extract increased GSH or TAS in kidney and liver tissues of rats and mice. However, the results also indicated that SOD content of RBC increased after five days of *Saliva triloba* intake as also reported in studies of (Bilto & Alabdallat, 2015a; 2015b; Alabdallat, 2021) and (Ajith *et al.*, 2007; Bakirel *et al.*, 2008; Asnani & Verma, 2009). They demonstrated that oral rosemary or ginger extract can significantly enhance Superoxide Dismutase (SOD) activity in mouse liver or diabetic rabbit serum. The current investigation also found that the tested plants did not reduce the red blood cell content of MDA after five days of treatment. This conclusion is supported the results of similar studies.

Conclusion

As our findings are based on volunteers with no history of oxidative stress, we can suggest the use of herbal extracts of plants like *Saliva triloba, Origanum syriacum* as medicinal herbs with antioxidant effects can improve the basal defense mechanism for oxidative stress, and this may help in decreasing oxidative stress related disease.

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Conflict of interest: None

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Ethics statement: This research was approved by the Jordan University Committee and therefore meets the ethical standards mentioned in the 1964 Declaration of Helsinki. Before participating in the study, each individual provided informed permission.

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