

## Efficacy of L-carnosine against *Schistosoma mansoni* antigens in liver, heart, kidney and brain of rabbits

Naima Z. Mohamed<sup>1</sup>, Monira A. Abd El Kader<sup>2</sup>, Sanaa A. Ali<sup>3\*</sup>

<sup>1</sup>Assistant professor, Therapeutic Chemistry Department, Pharmaceutical and Drug Industries Division,

<sup>2</sup>Assistant professor, Biochemistry Department, Genetic Engineering and Biotechnology Devision, National Research Centre, Dokki, Giza, Egypt.

<sup>3</sup>Professor Dr, Therapeutic Chemistry Department, Pharmaceutical and Drug Industries Division, National Research Centre, Dokki, Giza, Egypt.

---

### ARTICLE INFO

#### Article history:

Received on: 15/12/2012

Revised on: 05/01/2013

Accepted on: 19/01/2013

Available online: 28/01/2013

---

#### Key words:

antigens; DNA; RNA;  
DNA/RNA; ATP ase; Acetyl  
cholinesterase

---

### ABSTRACT

The present investigation was an attempt to study the enhancement effect of L-carnosine (beta alanyl-L-histidine) on the influence of vaccination on healthy (non-infected) rabbits treated with *Schistosoma mansoni* egg antigens, cercariae antigens, and worms antigens as protective agents against infection. This study involved individual injection of three *Schistosoma mansoni* antigens: soluble egg antigen (SEA), cercarial antigen preparation (CAP) and soluble worm antigen preparation (SWAP), in three rabbit groups, respectively. Three other groups each received the same specific antigen in conjunction with the administration of L-carnosine, biochemical parameters including DNA, RNA, DNA/RNA ratio concentrations in addition ATPase, and acetyl cholinesterase activities were measured in liver, heart, kidney and brain in all groups. Elevation in most parameters was observed in the immunized groups. Carnosine treatment of rabbit groups immunized with SEA, CAP and SWAP in comparison to the non-carnosine-treated immunized groups resulted in amelioration the changes of DNA, RNA, ATPase and acetyl cholinesterase activities in most groups. L-carnosine has a beneficial effect in the amelioration of the changes in biochemical parameters as a result of *S. mansoni* antigen immunization.

---

### INTRODUCTION

Since the pioneer works that introduced the basis of immunization as a powerful tool to prevent infectious diseases, the search of antigens that mediate protective immunity against parasites, has been a major goal of research in medical parasitology. It is thus envisioned that the development of effective vaccines could be relevant to control programs of largely endemic diseases (Tendler, 1987). Mice immunized with soluble worm antigen preparation (SWAP) and interleukin-12 show a highly statistically significant increase in resistance when compared with those immunized with SWAP only (Abdel-Aaty et al., 1999). Laboratory investigations of mechanisms of mammals' immunological responses have long been under intensive scrutiny. Leukocytes react directly with SEA and SWAP, through distinct intracellular signaling pathways, induce peripheral blood mononuclear cell proliferation (Hilpela et al., 2003). The products secreted by schistosome eggs captured in the hepatic

granulomata may promote angiogenesis within its granuloma by upregulating endothelial cell vascular endothelial growth factor (Loeffler et al., 2002). L-Carnosine (b-alanyl-L-histidine) is a naturally occurring dipeptide, that is endogenously synthesized, and widely found in the brain, muscle, kidney, stomach, and, in large amounts, in skeletal muscle (Guiotto et al., 2005). Carnosine has been proved to play a number of biological functions, including antioxidant activity, as a free radical scavenger, ability to chelate metal ion, anti-inflammatory and antisenesence properties (Kohen et al., 1988). In addition, carnosine is an inhibitor of protein glycosylation and may prevent the formation of the advanced glycation end-products (AGEs). Carnosine is a naturally-occurring dipeptide, comprised of the amino acids, beta-alanine and L-histidine. It is a strong free-radical scavenger capable of blocking free radical chain reactions, inhibiting cell damage. It is also essential for DNA and RNA polymerase activity to aid cell damage that is endogenously synthesized, and widely found in the brain, muscle, kidney, stomach, and, in large amounts, in skeletal muscle (Renner et al., 2010). Carnosine has been proved to play a number of biological functions, including antioxidant activity, as a free

---

\* Corresponding Author

Prof. Dr. Sanaa Ahmed Ali, Therapeutic Chemistry Department, National Research Center Cairo, Egypt 12622

Telephone: 00202 33371499; Fax: 00202 33370931

radical scavenger, ability to chelate metal ion, anti-inflammatory and antisenescence properties (Guiotto *et al.*, 2005). In addition, carnosine is an inhibitor of protein glycosylation and may prevent the formation of the advanced glycation end-products (AGEs) beta alanyl-L-histidine is present at surprisingly high levels (up to 20 mM) in muscle and nervous tissues in many animals. L-carnosine inhibits lipid peroxidation and oxidative modification of proteins in muscle tissue since it acts as a reactive oxygen species (ROS) scavenger (Hipkiss, 1998; Soliman *et al.*, 2006). It has been demonstrated to play a number of biological roles as an anti-inflammatory agent, free radical scavenger and protein glycosylation inhibitor (Alhamdani *et al.*, 2007; Decker *et al.*, 2000). More recently, it has been suggested that carnosine and homocarnosine protect neuronal cells against glutamate-induced toxicity (Boldyrev *et al.*, 2004). In addition, carnosine has been demonstrated to protect PC12 cells from A $\beta$ 42-induced neurotoxicity via regulation of glutamate release (Fu *et al.*, 2008). However, no information is yet available on the effect of carnosine and related compounds on ferritin-mediated DNA damage. In the current study, we examined the protective effects of carnosine and homocarnosine on ferritin/H<sub>2</sub>O<sub>2</sub> system-mediated DNA damage. Carnosine has been shown that *Fasciola* and *Schistosoma* worm antigens mixed with or without saponin as well as saponin alone are successful in protecting mice against *S. mansoni* infection. The combinations are more efficacious than saponin and *Fasciola* antigens alone (Maghraby *et al.*, 2010a). This protection is achieved by a reduction in the total number of male and female worms, as well as in the levels of toxins elaborated by them. The role of these antigens in eliminating the products of oxidative stress and assistance in immune-mediated destruction of eggs that ameliorate the histopathological picture of liver cells and preserve its function has been demonstrated (Maghraby *et al.*, 2010a). For example, in liver sections, egg granuloma size was reduced in animals vaccinated with *Fasciola* or *Schistosoma* eggs as well as *Fasciola* or *Schistosoma* eggs with saponin antigens (Maghraby *et al.*, 2010b). Carnosine has been postulated to act as a buffer to neutralize lactic acid produced in skeletal muscle that is undergoing anaerobic glycolysis. One of the most likely places for oxidative stress is the human brain. The brain uses about 20% of the oxygen consumed, has the highest rate of oxygen consumption of any organ, and contains lipids with a high content of easily oxidized unsaturated fatty acids (Kohen *et al.*, 1988). The present study was undertaken to evaluate the possible ameliorative effect of L-carnosine on vaccination induced alterations in DNA, RNA, DNA/RNA contents as well as adenosine triphosphatase (ATPase) and acetyl cholinesterase activities in liver, heart, kidney and brain in rabbits.

## MATERIALS AND METHODS

### Chemicals

All fine chemicals and the L-carnosine used were products of the Sigma Chemical Company, St. Louis, USA.

### Animals

Twenty-one male New Zealand white rabbits weighing approximately 2 kg were obtained in-house from the Research Institute of Ophthalmology, Cairo. They were routinely inspected for ecto- and endo-parasites.

Anesthetic procedures complied with the legal ethical guidelines approved by the Ethical Committee of the Federal Legislation and National Institutes of Health Guidelines in the United States, and were approved by the ethical committee of the National Research Centre in Egypt. An overdose of ether was given gradually to the rabbits to ensure that the animals did not suffer at the final stage of the experiment.

### Experimental design and immunizations

The rabbits were divided into seven groups of three rabbits each. Group 1 (G1) was designated the healthy control group. The six treated groups were divided into two large collections each comprised of three groups according to treatment. Batch A was comprised of groups 2, 3 and 4, each of which was injected with a specific antigen (egg, cercariae or worm antigens of *S. mansoni*) as follows: Group 2, SEA-I; Group 3, CAP-I, Group 4: SWAP-I. Batch B was comprised of groups 5, 6 and 7, each of which was injected with L-carnosine in addition to a specific antigen as follows: Group 5, SEA-I-C; Group 6, CAP-I-C; Group 7, SWAP-I-C. The six groups of rabbits (groups 2-7) were subcutaneously injected with 0.5 mg of the specified antigen formulated with an equal volume of Freund's complete adjuvant. A second booster dose of 1 mg in Freund's incomplete adjuvant (v/v) was injected on day 21.

A third booster dose of 1 mg in Freund's incomplete adjuvant (v/v) was injected on day 26. Sera were collected two days after the last immunization in groups 2 to 4. Groups 5 to 7 were injected with an intramuscular dose of L-carnosine at 100 mg/day for 15 days (Soliman *et al.*, 2003). Blood was collected from control and injected rabbits after decapitation. Samples were allowed to clot for two hours at room temperature and overnight at 4°C. After centrifugation at 100 x g for 15 minutes, sera were separated and stored at -20°C until used.

### Preparation of antigen

All antigens used for this research (cercariae, worm and egg antigens of *S. mansoni*) were obtained from the Theodore Bilharz Research Institute, Giza, Egypt. SEA, CAP and SWAP antigens of *S. mansoni* were prepared as previously described (Da-Silva and Ferri, 1968).

### Preparation of organs homogenate

Organs homogenate was prepared by homogenization 0.5 gm tissues in 10 ml of 0.25 M sucrose solution.

### Quantitative determination of organs DNA and RNA contents

Organs DNA and RNA contents were estimated according to the method of Sihigko *et al.*, (1967).

**Calculation**

DNA and RNA concentration were calculated in mg of DNA or RNA / gm of wet tissue.

$$\frac{\text{Reading of sample} - \text{Reading of blank} \times \text{Conc. of standard solution} \times \text{dilution factor}}{\text{Reading of standard solution} \times \text{Weight of tissue used}} \times 1 \text{ gm wet tissue}$$

**Adenosine triphosphatase assay**

The measurement of the enzyme was made using the method described by Chanez *et al.*, (1985).

0.05 ml of supernatant was added to 1.05 ml of 40 mM Tris Hcl containing 150 mM NaCl, 20 mM KCl and 5 mM MgCL<sub>2</sub> with pH 7.4. After preincubation for 5 min. at 37 °C the reaction was started by the addition of 0.04 ml of 4 mM Tris-ATP and stopped after 15 min. later by adding 1 ml of ice cold 10 % TCA. The mixture was centrifuged at 3000 r.p.m for 15 min. Inorganic phosphorus was determined in the aliquot of the supernatant.

**Determination of acetylcholinestrace (AChE)**

The procedure used in the present study for the determination of cholinesterase activity in the samples is a modification of the method of Ellman *et al.*, (1961) as described by Gorun *et al.*, (1978).The principle of the method is the measurement of the rate of production of thiocholine as acetylthiocholine is hydrolyzed.



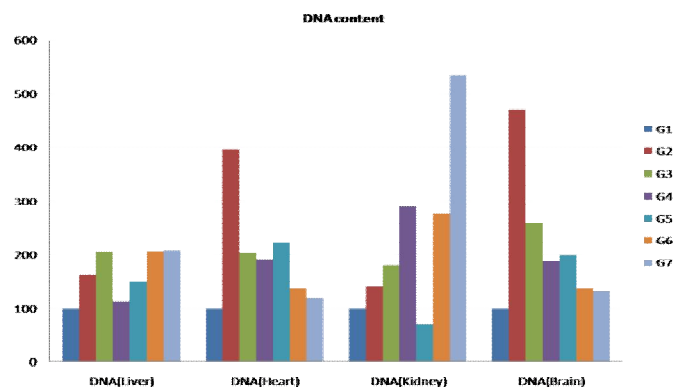
**Statistical analysis**

Data are expressed as means ± SD, and were analyzed using analysis of variance (ANOVA) (SPSS, Chicago, IL, USA).

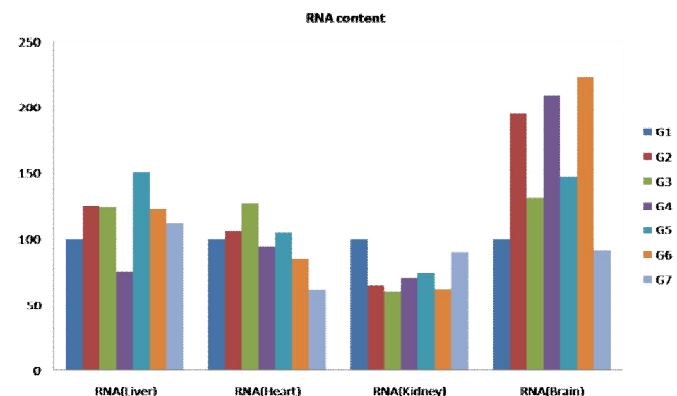
**RESULTS**

Table (1) & Figure (1) Show that DNA activities in heart & brain revealed a significant elevation after SEA, CAP and SWAP immunization with different percentage change, after treated with carnosine a significant reduction in all DNA activates with different percent, while SEA immunization in liver and kidney revealed a significant increase and carnosine treatment inhibited these elevation with 150% & 70% after 163% & 141% respectively as shown in table 1 and fig.1. Table (2) & Figure (2) RNA activity in heart significantly elevated after immunized with SEA, CAP and SWAP with 105.8%, 128% and 94.4% respectively and carnosine has a remarkable effect for reduction these elevations with 104.6%, 82.2% and 61.4% respectively. In brain SEA and SWAP immunization caused a significant elevation with 195.5% and 208.9% which decreased to 148% and 91.1% with given carnosine. Table (3) & Figure (3) DNA/RNA ratio carnosine illustrate a markedly reduction in the elevation caused by SEA immunization in liver, heart, kidney and brain with different percentage change. 130, 405, 217 and 243% respectively reduced to 100, 228.9, 95.7 and 136.8 respectively. In case of CAP-immunization a significant reduction by carnosine elevated in brain than the other organs reduced 206.6% to 65.8%. Table (4) &

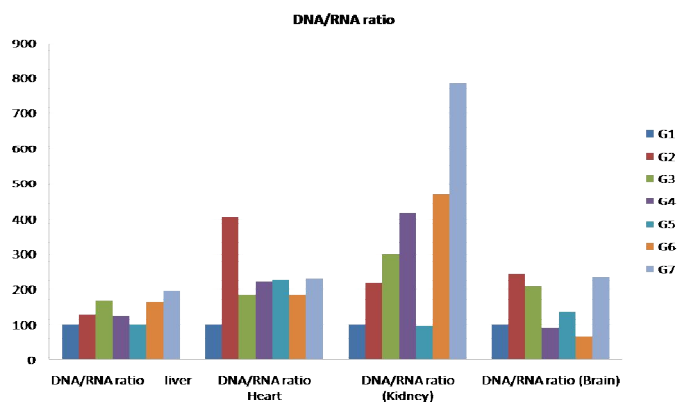
Figure (4) ATPase activities markedly elevated with SEA immunization in liver and kidney with percentage 372% and 316% percent change while significantly decreased in heart and brain with 30.5% and 52.1% respectively. Carnosine administration ameliorating these disturbances in the enzyme activities with different percent change. Table (5) & Figure (5) acetylcholinestrace activity revealed a highly significant elevation in kidney and brain 398% and 233% after immunized with SEA antigen, a markedly decrease in these activities levels 279.6% and 209.7% respectively, as a result of given carnosine.



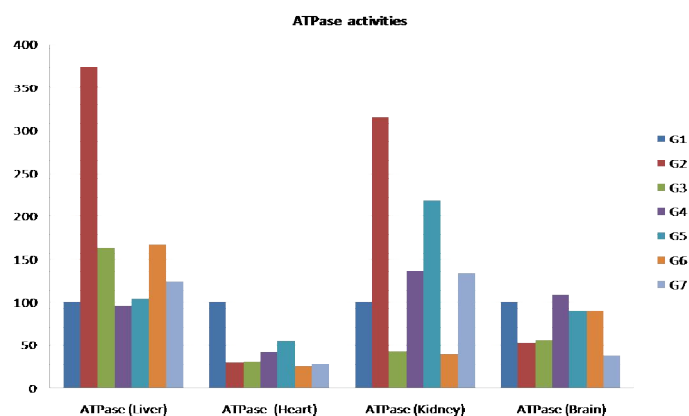
**Fig. 1:** Percent change of DNA contents in liver, heart, kidney and brain from rabbits immunized groups and immunized -treated with L-carnosine groups.



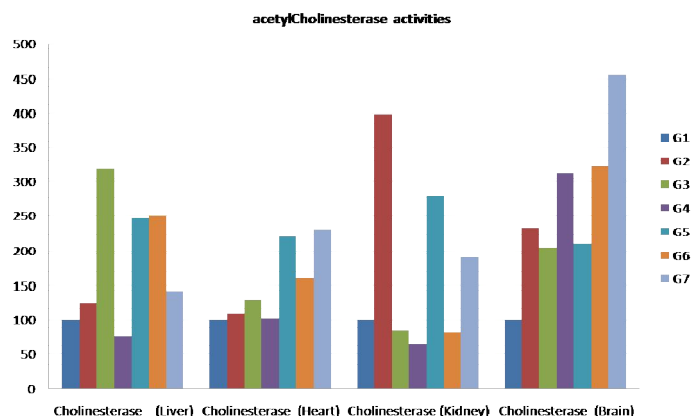
**Fig. 2:** Percent change of RNA contents in liver, heart, kidney and brain from rabbits immunized groups and immunized -treated with L-carnosine groups.



**Fig. 3:** Percent change of DNA/RNA ratio in liver, heart, kidney and brain from rabbits immunized groups and immunized -treated with L-carnosine groups.



**Fig. 4:** Percent change of ATPase activities in liver, heart, kidney and brain from rabbits immunized groups and immunized -treated with L-carnosine groups.



**Fig. 5:** Percent change of acetyl cholinesterase activities in liver, heart, kidney and brain from rabbits immunized groups and immunized -treated with L-carnosine groups.

**Table. 1:** Effect of L-carnosine on DNA in SEA, CAP and SWAP groups.

Organs	Control		Immunized groups				Treatment groups			ANOVA P ≤
	G <sub>1</sub>	SEA-I	CAP-I	SWAP-I	SEA-I-C	CAP-I-C	SWAP-I-C			
		G <sub>2</sub>	G <sub>3</sub>	G <sub>4</sub>	G <sub>5</sub>	G <sub>6</sub>	G <sub>7</sub>			
Liver	0.182±0.037 (3,6,7)	0.297±0.068 -	0.373±0.050 (1,4)	0.206±0.014 (3,6,7)	0.273±0.087 -	0.376±0.159 (1,4)	0.377±0.096 (1,4)	0.053		
Heart	0.140±0.007 (2,3,4,5)	0.554±0.071 (1,3,4,5,6,7)	0.285±0.076 (1,2,6,7)	0.268±0.056 (1,2,7)	0.31±0.045 (1,2,6,7)	0.193±0.03 (2,3,5)	0.17±0.004 (2,3,4,5)	0.001		
Kidney	0.161±0.031 (3,4,6,7)	0.227 ±0.05 (4,5,6,7)	0.289±0.065 (1,4,5,6,7)	0.468±0.011 (1,2,3,5,7)	0.112±0.033 (2,3,4,6,7)	0.448±0.116 (1,2,3,5,7)	1.022±0.074 (1,2,3,4,5,6)	0.001		
Brain	0.119±0.009 (2,3,5)	0.56±0.118 (1,3,4,5,7)	0.31±0.065 (1,2,6,7)	0.224±0.037 (1,2)	0.237±0.056 (1,2)	0.164±0.006 (2,3)	0.182±0.06 (2,3)	0.001		

- Data are expressed as means ± SD of rabbits in each group as follows: I = immunized by antigen; I-C = immunized and L-carnosine- treated
- DNA expressed as μmoles/100mg tissue weight
- Analysis of data was performed by one-way analysis of variance (ANOVA) accompanied by *post hoc* least significant difference (LSD; SPSS computer programme), the significance values at  $P < 0.05$ . All the values are compared with the control group.
- Number of groups which have a significant correlation between each other.

**Table. 2:** Effect of L-carnosine on RNA in SEA, CAP and SWAP groups.

Organs	Control		Immunized groups			Treatment groups			ANOVA P ≤
	G <sub>1</sub>	SEA-I	CAP-I	SWAP-I	SEA-I-C	CAP-I-C	SWAP-I-C		
		G <sub>2</sub>	G <sub>3</sub>	G <sub>4</sub>	G <sub>5</sub>	G <sub>6</sub>	G <sub>7</sub>		
Liver	0.790 ±0.04 (5)	0.997±0.23 -	0.991±0.122 -	0.589±0.107 (5)	1.191±0.10 (1,4)	0.975±0.265 -	0.886±0.25 -	0.230	
Heart	0.345±0.031 (7)	0.365±0.024 (7)	0.443±0.12 (6,7)	0.326±0.032 -	0.361±0.049 (7)	0.294±0.03 (3)	0.212±0.129 (1,2,3,5)	0.510	
Kidney	0.696±0.073 (2,3,4,5,6)	0.453±0.051 (1)	0.421±0.034 (1,7)	0.492±0.072 (1)	0.517±0.069 (1)	0.429±0.07 (1,7)	0.624±0.217 (3,6)	0.035	
Brain	0.157±0.049 (6)	0.307±0.059 -	0.207±0.12 -	0.328±0.059 (7)	0.233±0.051 -	0.351±0.177 (1,7)	0.143±0.123 (4,6)	0.135	

- Data are expressed as means ± SD of rabbits in each group as follows: I = immunized by antigen; I-C = immunized and L-carnosine- treated
- RNA expressed as μmoles/100mg tissue weight
- Analysis of data was performed by one-way analysis of variance (ANOVA) accompanied by *post hoc* least significant difference (LSD; SPSS computer programme), the significance values at  $P < 0.05$ . All the values are compared with the control group.
- Number of groups which have a significant correlation between each other.

**Table. 3:** Effect of L-carnosine on the ratio of DNA/RNA ratio in SEA, CAP and SWAP groups.

Organs	Control		Immunized groups			Treatment groups			ANOVA P ≤
	G <sub>1</sub>	SEA-I	CAP-I	SWAP-I	SEA-I-C	CAP-I-C	SWAP-I-C		
		G <sub>2</sub>	G <sub>3</sub>	G <sub>4</sub>	G <sub>5</sub>	G <sub>6</sub>	G <sub>7</sub>		
Liver	0.23±0.04 (7)	0.30±0.05 -	0.38±0.07 -	0.29±0.03 (7)	0.23±0.12 (7)	0.37±0.13 -	0.45±0.29 (1,4)	0.229	
Heart	0.38±0.04 (1, 5, 7)	1.54±0.29 (1,3,4,5,6,7)	0.70±0.37 (2)	0.84±0.24 (2)	0.87±0.24 (1, 2)	0.70±0.13 (2)	0.88±0.39 (1, 2)	0.007	
Kidney	0.23±0.03 (4, 6, 7)	0.50±0.12 (7)	0.69±0.20 (7)	0.96±0.11 (1,5,7)	0.22±0.03 (4,6,7)	1.08±0.391 (1,5,7)	1.81±0.94 (1,2,3,4,5,6)	0.003	
Brain	0.76±0.13 (2,3,7)	1.85±0.35 (1,6)	1.57±1.3 (1,4,6)	0.69±0.11 (3)	1.04±0.30 -	0.50±0.23 (2,3,7)	1.79±0.89 (1,6)	0.030	

- Data are expressed as means ± SD of rabbits in each group as follows: I = immunized by antigen; I-C = immunized and L-carnosine- treated
- Analysis of data was performed by one-way analysis of variance (ANOVA) accompanied by *post hoc* least significant difference (LSD; SPSS computer programme), the significance values at  $P < 0.05$ . All the values are compared with the control group.
- Number of groups which have a significant correlation between each other.

**Table 4:** Effect of L-carnosine on ATPase in SEA, CAP and SWAP groups.

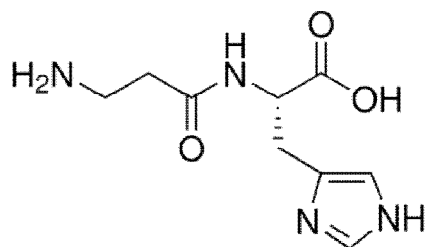
Organs	Immunized groups							ANOVA P ≤
	Control	Immunized groups			Treatment groups			
	G <sub>1</sub>	SEA-I G <sub>2</sub>	CAP-I G <sub>3</sub>	SWAP-I G <sub>4</sub>	SEA-I-C G <sub>5</sub>	CAP-I-C G <sub>6</sub>	SWAP-I-C G <sub>7</sub>	
Liver	0.025±0.004 (4)	0.093±0.40 (1,3,4,5,6,7)	0.041±0.006 (2)	0.024±0.006 (2)	0.026±0.005 (2)	0.042±0.011 (2)	0.031±0.023 (2)	0.200
Heart	0.092±0.061 (2,3,4,6,7)	0.028±0.004 (1)	0.029±0.003 (1)	0.038±0.008 (1)	0.050±0.011 -	0.023±0.003 (1)	0.026±0.011 (1)	0.039
Kidney	0.043±0.005 (2)	0.136±0.023 (1,3,4,5,6,7)	0.018±0.003 (2,4,5,7)	0.058±0.003 (2,3,5,6)	0.094±0.014 (1,2,3,4,6,7)	0.017±0.003 (2,4,5,7)	0.057±0.033 (2,3,5,6)	0.001
Brain	0.048±0.007 (5)	0.025±0.009 (5)	0.027±0.002 (5)	0.052±0.006 (5)	0.043±0.050 (1,2,3,4,6,7)	0.043±0.004 (5)	0.018±0.006 (5)	0.001

- Data are expressed as means ± SD of rabbits in each group as follows: I = immunized by antigen; I-C = immunized and L-carnosine- treated
- ATPase expressed as μmole/mg tissue weight
- Analysis of data was performed by one-way analysis of variance (ANOVA) accompanied by *post hoc* least significant difference (LSD; SPSS computer programme), the significance values at  $P < 0.05$  All the values are compared with the control group.
- Number of groups which have a significant correlation between each other.

**Table 5:** Effect of L-carnosine on Acetyl cholinesterase in SEA, CAP and SWAP groups.

Organs	Immunized groups							ANOVA P ≤
	Control	Immunized groups			Treatment groups			
	G <sub>1</sub>	SEA-I G <sub>2</sub>	CAP-I G <sub>3</sub>	SWAP-I G <sub>4</sub>	SEA-I-C G <sub>5</sub>	CAP-I-C G <sub>6</sub>	SWAP-I-C G <sub>7</sub>	
Liver	0.059±0.008 (3,5,6)	0.073±0.006 (3,4,5,6)	0.188±0.019 (1,2,4,5,6,7)	0.044±0.005 (2,3,5,6,7)	0.145±0.022 (1,2,3,4,7)	0.147±0.004 (1,2,3,4,7)	0.083±0.029 (3,4,5,6)	0.001
Heart	0.077±0.047 (5,7)	0.083±0.009 (5,7)	0.099±0.055 (5,7)	0.078±0.011 (5,7)	0.17±0.020 (1,2,3,4,7)	0.123±0.11 (7)	0.187±0.005 (1,2,3,4,5,6)	0.001
Kidney	0.093±0.011 (2,5,7)	0.37±0.056 (1,3,4,5,6,7)	0.078±0.011 (2,5,7)	0.043±0.007 (2,5,7)	0.26±0.049 (1,2,3,4,6,7)	0.075±0.006 (2,5,7)	0.178±0.017 (1,2,3,4,5,6)	0.001
Brain	0.359±0.045 (2,3,4,5,6,7)	0.838±0.167 (1,3,4,7)	0.733±0.054 (1,4,6,7)	1.123±0.013 (1,2,3,5,7)	0.753±0.148 (1,4,6,7)	1.158±0.012 (1,2,3,5,7)	1.636±0.097 (1,2,3,4,5,6)	0.001

- Data are expressed as means ± SD of rabbits in each group as follows: I = immunized by antigen; I-C = immunized and L-carnosine- treated
- Acetyl cholinesterase expressed as (U/g).
- Analysis of data was performed by one-way analysis of variance (ANOVA) accompanied by *post hoc* least significant difference (LSD; SPSS computer programme), the significance values at  $P < 0.05$ . All the values are compared with the control group.
- Number of groups which have a significant correlation between each other.

**Fig. 6:** Chemical structure of Carnosine.

## DISCUSSION

In the present study, the treatment of rabbit with carnosine has been designated as protective mediator from *Schistosoma mansoni* egg antigens induced dysfunction of some enzymes. This finding evidenced by the observed improvement of most examined biomarkers including DNA and RNA contents DNA/RNA ratio in addition ATPase and acetyl cholinesterase activities.

The foregoing immunological results support the relative actions of the three antigens. However, the authors stated that the histopathological picture of SWAP-C-treated animals showed a greater immunological defence in lymph nodes' cellular reaction, presented as sinus histiocytosis (Soliman *et al.*, 2002). Nassr *et al.* recorded that anti-SWAP IgG1 and IgG4 were increased in schistosomiasis (Nassr *et al.*, 2002). However, to potentiate the SEA vaccine action against schistosomiasis, combined

administration of SEA in conjunction with 28 kDa glutathione-S-transferase antigens in infected animals was suggested (Lebens *et al.*, 2003). Nevertheless, the above-mentioned conservation of hepatic glycogen and phosphorylase by carnosine combating the high antigen doses could be ascribed to its well-documented antioxidant action (Soliman *et al.*, 2006; Ali, 2012). This apparently contradicts its decreasing effect on the tested serum parameters, which could be ascribed to a pro-oxidant effect. Pro-oxidant effects were previously recorded for other antioxidant agents as well as L-carnosine when given in high dosages, for example vitamin C (Paolini *et al.*, 1999). L-carnosine is a potent and selective scavenger of alpha, beta-unsaturated aldehydes, typical by-products of membrane lipid peroxidation (considered second messengers of the oxidative stress response), and inhibits aldehyde-induced protein-protein and DNA-protein cross-linking in neurodegenerative disorders such as Alzheimer's disease (Guiotto *et al.*, 2005). L-carnosine involvement in the activation of natural systems of host immune resistance has been reported. It induced liberation of the immune modulator intermediates, cytokines and interleukins. It could also bind to immune system cell receptors that stimulated the liberation of hepatocyte growth factor and cytokines, causing liver recovery (Soliman and Ali, 2003).

Because RNA is an essential component of protein synthesis, its concentration in tissue often reflects the rate of protein synthesis. The RNA: DNA ratio provides an index of

protein synthetic capacity per cell since the amount of DNA per cell is assumed not to vary with condition or with growth rate, Changes in DNA: RNA ratios indicate alterations in transcription and translation processes. A decrease in transcription and translation processes will affect overall concentration of structural and functional proteins (enzymes) (Wanger et al., 1998). Carnosine protects rabbit hearts from reperfusion injury after ischemia, also as a physiological activator for myosin ATPase (Kohen et al., 1988). Natural defense mechanisms vary from one species to another and within the tissues of the same species. Skeletal muscle and brain are two of the tissues that have the most active oxidative metabolism, yet the concentrations of the antioxidants vitamin E and vitamin C in these tissues are not particularly high (Kohen et al., 1988). It also promoted liver regeneration in partially hepatectomized mice, which was shown in highly significant increases in weight, RNA content, and many hepatic proteins. The modulation of host immune response against SEA by L-carnosine could be comparable to the immune modulation of *S. mansoni* egg recorded by immunomodulators (Jakubzick et al., 2004 & Leinonen et al., 2004). Carnosine and homocarnosine compounds effectively inhibited ferritin/ H<sub>2</sub>O<sub>2</sub>-mediated hydroxyl radical generation and decreased the mutagenicity of DNA induced by the ferritin/H<sub>2</sub>O<sub>2</sub> reaction (Guiotto et al., 2005). Therefore, carnosine has the potential of being a drug to prevent and treat senile cataract and to delay eyesight senescence, which is one of the manifestations of aging. The pharmacological effects of carnosine seem to due to its penetration into the lens then boosting the antioxidant ability of the lens, increasing the activity of Na,K-ATPase (Iovine et al., 2012). The small number of deviated parameters in SEA-I-C, CAP-I-C and SWAP-I-C in DNA & RNA Liver animals might reflect an inherited ability of the animal's body to combat the adult worm. The decrease of almost parameters in all *Schistosoma mansoni* antigens animals, can be attributed to the biological interrelations between both parasite and host tissues. Also, the high (experimental) dosages of antigen may not have matched the corresponding amounts in natural infestation. The natural short time-span of both developmental stages (*i.e.*, eggs and cercariae which are transient in the liver) in host tissues support this explanation. In conclusion, immunological studies should investigate further the effect of smaller dosages of L-carnosine combined treatment. The selectivity of L-carnosine proved favorable DNA, RNA, ATPase, and acetyl cholinesterase. It is expected that smaller dosages may be able to normalize most tested parameters.

#### ACKNOWLEDGEMENT

The authors would like to appreciate soul of Prof. Kawther Soliman, Medical Biochemistry, Faculty of Medicine, Cairo University for giving the financial support of this research.

#### Conflict of Interests

No conflict of interests is declared.

#### REFERENCES

- Abdel-Aaty HE, Ramadan NI, Mahmoud MS, Abdel-Aziz SS, Khalil, H.M., El-Badawy, N.M., Khalil, HH, Role of recombinant interleukin-12 as an adjuvant on vaccine-induced immunity in murine *Schistosoma mansoni* infection. J Egypt Soc Parasitol 1999, 29, 1-11.
- Alhamdani M S, Al-Kassir A H, Abbas F K, Jaleel N A. and Al-Tae, M. F. Antiglication and antioxidant effect of carnosine against glucose degradation products in peritoneal mesothelial cells. Nephron. Clin. Pract. 2007;107, c26-34.
- Ali SA. Evaluation of the immunological effect of beta alanyl-L-histidine against *Schistosoma mansoni* antigens in rabbits J Infect Dev Ctries. 2012, 6(2), 166-175.
- Boldyrev, A., Bulygina, E., Leinsoo, T., Petrushanko, I., Tsubone, S., Abe, H., Protection of neuronal cells against reactive oxygen species by carnosine and related compounds. Comp. Biochem. Physiol. 2004, 137, 81-88.
- Chanez, C., Floxor, A.M., Hamon, M. Long lasting effects of intra uterine growth retardation on basal and 5-HT-stimulated Na<sup>+</sup>, K<sup>+</sup>-ATPase in the brain of developing rats. Neurochem.Int. 1985, 7 (2), 319-329.
- Da-Silva LC, Ferri RC. *Schistosoma mansoni* homogenate for active immunization of mice. Amer J Trop Med Hyg 1968, 17, 367-371.
- Decker EA, Livisay S A, Zhou S. A re-evaluation of the antioxidant activity of purified carnosine. Biochemistry (Mosc) 2000, 65, 766-770.
- Ellman G L, Courtney KD, Andres V, Featherstone RM. A new and rapid colorimetric determination of acetylcholinesterase activity. Biochem. Pharmacol., 1961, 7, 88-95.
- Fu Q, Dai H, Hu W, Fan Y, Shenn Y, Zhang W, Chen Z. Carnosine protects against Abeta41-induced neurotoxicity in differentiated rat PC12 cells. Cell Mol. Neurobiol. 2008, 28, 307-316.
- Gorun V, Proinov I, Baltescu V, Balaban G, Barzu O. Modified Ellman procedure for assay for cholinesterase in crude enzymatic preparation. Anal. Biochem., 1978, 86, 324-326.
- Guiotto A, Calderan A, Ruzza P, Borin G. Carnosine and carnosine-related antioxidants: a review Curr Med Chem 2005, 12, 2293-2315.
- Hilpela, P., Oberbanscheidt, P., Hahne, P., Hund, M., Kalhammer, G., Small, J.V., Bahler, M. SWAP-70 identifies a transitional subset of actin filaments in motile cells. Mol Biol Cell 2003, 14, 3242-53.
- Hipkiss A R. Carnosine, a protective, anti-ageing peptide. Int. J. Biochem. Cell Biol. 1998, 30, 863-868.
- Iovine B, Iannella ML, Nocella F, Pricolo MR, Bevilacqua MA. Carnosine inhibits KRAS-mediated HCT116 proliferation by affecting ATP and ROS production Cancer Letters 2012, 315, 122-128
- Jakubzick C, Wen H, Matsukawa A, Keller M, Kunekel SL, Hogbova N. Role of CCR4 Ligands, CCL17 and CCL22 during *Schistosoma mansoni* egg induced pulmonary granuloma formation. Am J Pathol. 2004, 165, 1211-1221.
- Kang JH. Protective effects of carnosine and homocarnosine on ferritin and hydrogen peroxide-mediated DNA damage BMB reports. 2010, 683-687.
- Kohen R, Yamamoto Y, Cundy KC, Bruce N, Ames BN. Antioxidant activity of carnosine, homocarnosine, and anserine present in muscle and brain Proc. Natl. Acad. Sci. 1988, 85, 3175-3179.
- Lebens M, Sun JB, Sadeghi H, Backstrom M, Olsson I, Mielcarek N, Li BL, Capron A, Czerkinsky C, Holmgren J. A mucosally administrated recombinant fusion protein vaccine against schistosomiasis protecting against immunopathology and infection. Vaccine 2003, 21, 514-520.
- Leinonen JS, Saari KA, Seppanen JM, Myllyla HM, Rajaniemi HJ. Immunohistochemical determination of carbonic anhydrase isoenzyme VI (CAVI) expression in lower airways. J Histochem Cytochem 2004, 52, 1107-1112.
- Loeffler DA, Lundy SK, Singh KP, Gerard HC, Hudson AP, Boros DL. Soluble egg antigens from *Schistosoma mansoni* induce angiogenesis-related processes by up-regulating vascular endothelial

growth factor in human endothelial cells. *J Infect Dis.* 2002, 185, 1650-1656.

Maghraby AS, Hamed MA, Ali SA. Bioimmunological response to *Schistosoma mansoni* and *Fasciola gigantica* worm homogenates either mixed with or without saponin. *J Infect Dev Ctries* 2010a, 4, 334-344.

Maghraby AS, Hamed MA, Aly HF, Ali SA. Antischistosomal activity of *Fasciola gigantica* eggs influenced by Egyptian saponin extracted from *Atriplex nummularia*. *J Am Sci.* 2010b, 6, 368-381.

Miriam Tendler. *Schistosoma Mansoni*: Protective antigens Mem.Inst.Oswaldo Cruz.Rio de Janeiro. Intern.Symp. on Schistosomiasis. 1987, 82, 125-128

Nagasawa T, Yonekura T, Nishizawa N, Kitts D D. *In vitro* and *in vivo* inhibition of muscle lipid and protein oxidation by carnosine. *Mol Cell Biochem.* 2001, 225, 29.

Nassr AKH, Hassan MM, Abdel Salam FM, Lashin AH, Shahin WA, Amin H. IgG isotypes in schistosomiasis patients before and after praziquantel. *J Egypt Soc Parasitol.* 2002, 32, 931-952.

Paolini M, Pozzetti L, Pedulli GF, Marchanarchesi F, Cantelli-Forti G. The nature of pro-oxidant property of vitamin C. *Life Science.* 1999, 64, 273-278.

Renner C, Asperger A A, Seyffarth J, Meixensberger R, Gebhardt F, Gaunitz. Carnosine inhibits ATP production in cells from malignant glioma. *Neurol. Res.* 2010, 1, 101-105.

Sihigko P, Korivistoenen C, Tratnyek A, Newball C, Friedman L. Quantative estimation of DNA and RNA in blood and liver homogenate. *Anal.Biochem.*, 1967, 19,514-519.

Soliman K, Abdel-Aziz M, Nassar Y, Abdel-Sattar ., El-Ansary A. Effects of carnosine on bilharzial infestation in hamsters: biochemical and histochemical studies. *Comp Biochem Physiol.* 2002, 132, 535-542.

Soliman K, Abo-El\_Doual S, Marei N. Effect of carnosine administration on the immune response in rabbit to *Schistosoma mansoni* antigens. *J Egypt Soc Prasiat.* 2003, 33, 663-678.

Soliman K M, Ali HF. Stimulatory effect on serum proteins in normal and partially hepatectomized mice. *Egypt J Physiol.* 2003, 25, 7-28.

Soliman KM, Hamed AM, Ali SA. Hepatoprotective Effect of Carnosine on Liver Biochemical Parameters in Chronic Ethanol Intoxicated Rat. *J Med Sci .* 2006, 6, 528-536.

Wang AM, Ma C Z H, Xie Z H, Shen F. Use of Carnosine as a Natural Anti-senescence Drug for Human Beings. *Biochemistry (Moscow)*, 2000, 65 (7), 869-871.

Wanger W, Durbin E, Buckley L. RNA: DNA ratios as indicators of nutritional condition in the copepod *Calanus finmarchicus*. *Mar Ecol Prog Ser.* 1998, 162, 173-181.

#### How to cite this article:

Naima Z. Mohamed, Monira A.Abd El Kader, Sanaa A. Ali., Efficacy of L-carnosine against *Schistosoma mansoni* antigens in liver, heart, kidney and brain rabbits. *J App Pharm Sci.* 2013; 3 (01): 039-045.