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Growth Performance, Liver and Kidney Function, Lipid Metabolism and Thyroid Hormones of Growing Rabbits Treated with Different Types of Metabolic Agents

Hamad, M. E.[1]; G. Ashour[2]; Sh. A. Gabr[1]; G. E. Younan[3] and Doaa A. Kamel[1]
1-Animal Production Department, Faculty of Agriculture, Tanta University, Egypt.
2-Animal Production Department, Faculty of Agriculture, Cairo University, 12613 Giza, Egypt.
3-Animal Production Research Institute, Agricultural Research Center, Dokki, Giza, Egypt.

ABSTRACT

Aim of the present study was to evaluate the effect of treatment of L-carnitine or coenzyme Q10 on growth performance, liver and kidney functions, thyroid hormones, and economic feed efficiency of growing rabbits fed diet supplemented with propolis. Total of 60 weaned New Zealand white rabbits (5 wk of age and 702.58±12.70 g live body weight) were divided into 3 similar groups (20 in each, 10 from each sex). Rabbits in the 1st group were fed commercial pelleted diet (CPD) without any treatment and served as control (G1). While, rabbits in the 2nd and 3rd groups were fed CPD (18% CP, 13% CF and 2800 Kcal/kg) supplemented with 0.5 g propolis (PR)/kg and orally administrated with 10 mg CoQ10/kg LBW (G2) and 40 mg L-carnitine (LC)/kg LBW (G3), respectively. Feeding rabbits was *ad. Libitum*, while drinking water nipples were present in each cage. From 5-13 wk of age as an experimental period, rabbits were treated by each combination twice weekly. Average of body weight (LBW), feed intake (FI) and daily gain (ADG), rate of feed conversion (FC) and viability, relative growth rate (RGR) and performance index (PI) were determined. At 13 weeks of age (end of experiment), blood samples were taken from 3 slaughtered males in each group to determine total proteins (TP), albumin (AL), creatinine (CR), urea (UR), cholesterol (CH), HDL, LDL and triglycerides (TG) concentrations, AST and ALT activity and T3 and T4 concentrations. Weights of liver, kidney and body fat were recorded. Small samples from liver and kidney tissues were taken to examine the histological structure. Results showed that final LBW, ADG, FI, RGR and FCR were not significantly affected by treatment, although these parameters tended to be the highest in G2, moderated in G3, and the lowest in G1, being higher in male than female rabbits. All growth performance parameters was not significantly affected by the interaction between treatment and sex of rabbits. Effect of treatment was not significant on absolute and relative weight of the liver and kidney. Effects of treatment on concentrations of TP, AL, GL, CR, UR, CH, HDL, LDL, TG, T3, T4, AL/GL ratio and ALT activity in blood serum were not significant, while AST activity reduced ($P<0.05$) in G2 and G3 than in G1. Based on the histological examination, rabbits in treated groups (G2 and G3) showed normal liver and kidney functions. Average weight of abdominal fat was higher ($P<0.05$) in G1 than in G2 and G3. Subcutaneous fat as absolute or relative weight of total fat was not significant. In conclusion, treatment of growing rabbits during marketing period (5-13 wk of age) with a combination of propolis and coenzyme Q10 or L-carnitine twice/week led to functional liver and kidney with normal lipid profile. These findings were associated with remarkable improvement in growth performance parameters.
Keywords: *Rabbit, propolis, coenzyme Q10, L-carnitine, growth, liver, kidney, fat.*

INTRODUCTION

The New Zealand White (NZW) rabbit is a commercial meat rabbit breed introduced into Egypt to participate in increasing meat production.NZW rabbits had high fertility, fecundity and prolificacy, and rapid growing. Under the Egyptian conditions, these advantages are affected to a great extent by several factors such as the environmental and management conditions (Yamani *et al*., 1991). Rabbit production is being encouraged as a means of improving the daily protein intake of individuals, because its high protein and low cholesterol content (Okonkwo *et al.,* 2008).

High levels of functional mitochondria (MIT) are required for energy production needed to cell meiotic process (May-Panloup *et al*., 2007). Body energy level was reduced by insufficient or dysfunction of mitochondria (May-Panloup *et al*., 2005). The process of aerobic metabolism produces reactive oxygen species (ROS), which are a natural and important part of many physiological processes. MIT are particularly susceptible to damage, in part due to their proximity to the source of ROS generation. Damaged MIT can create a self-perpetuating cycle as defective respiration leads to a further increase in ROS, then the energy-intensive processes of cell can be impaired (Pritchard *et al*., 2015). MIT play a key role in the physiology of eukaryotic cells during all stage of life and their main function is to provide cells with ATP through oxidative phosphorylation (Cummins, 2004; Smith *et al.,* 2005). Mitochondrial dysfunction may lead to incomplete detoxification of the free radicals, which may lead to oxidative damage to macromolecules such as lipids, proteins, and DNA (Abdelrazik *et al.,* 2009).

A special interest has been developed for natural products with metabolic and antioxidant capacity and beneficial effects on animal health. Some of these products are propolis, coenzyme Q_{10} and L-carnitine. Propolis (PR) is a complex resinous material that honey bees (*Apis mellifera*) produce from the exudates of various plants. Propolis has high content of polyphenolic composites (flavonoids, tannins, terpenoids and phenolic compounds), and also has an antioxidant properties (Ramos and Miranda, 2007; Seven *et al*., 2011). The antioxidant activity of phenolics is mainly due to their redox properties, which allows them to act as reducing agents, hydrogen donators, singlet oxygen quenchers and metal chelators (Ivanova *et al.,* 2005). In heat stressed broilers, several invistigators suggested that PR seems to inhibit stress of oxidation (Seven *et al*., 2011).

L-carnitine (LC), as a polar natural, compound is vitamin-like amino-acid synthesized within the body of most animals from lysine and methionine (Groff and Gropper, 2000), playing a vital role in the detoxification in the cell (Arrigoni-Martelli and Caso, 2001) and important for carrying long-chain fatty acids to MIT during lipid metabolism for ATP production (Hoppel,

2003; Abdelrazik *et al.*, 2009). Also, as an antioxidant, LC prevent the oxidative damages of the cell membranes (Marasli *et al*., 2005; Rizzo *et al*., 2010). The positive effect of LC as dietary supplements on growth performance of bulls was indicated by Abdel-Khalek *et al*. (2015) and in cattle (Carlson *et al*., 2006).

Coenzyme Q10 (CoQ10) is a fat soluble vitamin-like substance present in every cell of the body and serves as a coenzyme for several of the key enzymatic steps of energy production(Kapoor and Kapoor, 2013). In mice, CoQ10 had a beneficial role in metabolism, antioxidant system and lipid peroxidation in the cell (Hosseinzadeh et al., 2015), electron transport chain in MIT and synthesis of ATP (Abdulhasan et al., 2015). Also, CoQ10 protects cell membrane stability and DNA oxidative damage, beside helping vitamin E recycling and maintaining the healthy energy levels (El‐Tohamy *et al*., 2012).

No available information in the literature regard to the effect of combinations of propolis, L-carnitine or coenzyme Q10 on growth efficiency and carcass quality of NZW growing rabbits in Egypt. The aim of the present study was to invistigate the effect of twice weekly oral treatment of L-carnitine or coenzyme Q10 on growth performance, liver and kidney function, thyroid hormones and economic feed efficiency of growing rabbits fed diet supplemented with propolis.

MATERIALS AND METHODS

The present experiment was conducted at rabbit private farm, Gharbia governorate, in co-operation with Faculty of Agriculture, Dapartment of Animal Production, Tanta University, during the period from April to May, 2016.

Total of 60 weaned exported rabbits (New Zealand White, NZW) were randomly alloted to 3 similar groups (10 males and 10 females in each). At the beginning of the experiment, the experimental rabbits aged 5 weeks, weighed 702.58±12.70 g as average live body weight (LBW) and were kept in wire cages (2 rabbits per cage, in 20 x 45 x 30 cm) with 10 replicates (five replicates for each sex) with suitable ventilation. All rabbit groups were kept under the same managerial conditions.

Rabbits in the 1st group were fed commercial pelleted diet (CPD) containing 18% CP, 13% CF and 2800 Kcal/kg without any treatment and served as control group (G1). While, rabbits in the 2nd and 3rd groups were fed CPD supplemented with 0.5 g propolis (PR)/kg and orally administrated with 10 mgCoQ10/kg LBW (G2) and 40mg LC/kg LBW (G3), respectively.

Propolis was added to the diet in a powder form, while each of CoQ10 or LC was dissolved in distilled water (1.5 ml/kg LBW). Rabbits in all experimental groups were fed *ad. libitum* and water was available through water nipple in each cage. Rabbits were treated twice weekly by each combination from 5 up to 13 wk of age.

Throughout the feeding period from 5 to 13 weeks of age, growth performance parameters including LBW and feed intake were recorded. Average daily gain and feed conversion ratio were also calculated. During the experimental period, viability rate, relative growth rate (RGR) and performance index (PI) were calculated as the following: *RGR (%) = (W2-W1)/½ (W2+W1) x 100.* Whereas: W1=initial LBW and W2 = final LBW. *PI = (Final LBW (kg)/feed conversion ratio) x100.*

At 13 weeks of age (end of the experiment), blood samples were taken from three slaughtered male rabbits from each group. Blood samples were collected into non-heparinized test tubes and serum was isolated by centrifugation at 3000 rpm for 15 min and kept at freezing temperature (-20^{o}C) until analyses. Total proteins, albumin, creatinine, urea, cholesterol, high density lipoproteins (HDL), low density lipoproteins (LDL) and triglycerides concentrations, AST and ALT activity and T3 and T4 concentrations in blood serum were determined. Spectrophotometer and commercial kits (Bio-Merieux, Laboratory Reagents and Products, France) were used for determination of some biochemicals in blood serum. Thyroid hormoned (T3 and T4) were assayed by direct radioimmunoassay technique (RIA) using ready antibody coated tubes kits.

After slaughter, weights of liver and kidney separated from each carcass were recorded. Abdominal and subcutaneous fats were isolated and weighed. Small samples from liver and kidney tissues were taken and put in neutral formalin (10% formalin solution, 38-40%) for 24-48 h, then washed by tap water for 24 h. Theereafter, samples were dehydrated (degraded levels of ethyl alcohol, 50 to 100%), cleared, sectioned by microtome (6-8 µm in thickness), and stained (hematoxyline and eosin). Light microscope (x 100 and 400) was used for examination of the histological structure of liver and kidney.

All data were statistically analyzed by analysis of variance (ANOVA) using General linear Model Program (SAS, 2004). The significant differences among means were set at P≤0.05 level using Duncan's Multiple Range Test procedure (Duncan, 1955).

RESULTS AND DISCUSSION

Growth performance of growing rabbits:
Effect of treatment:

Growth performance parameters, including final live body weight (LBW), averages of daily gain (ADG) and feed intake (ADFI), relative growth rate (RGR) and feed conversion ratio (FCR) were not significantly affected by treatment, although these parameters tended to be the highest in G2, moderated in G3, and the lowest in G1. This trend was reflected in significant (P<0.05) increase in performance index (PI) in G2 and G3 than in G1, with the highest viability rate of rabbits in G2. Growth performance parameters, including LBW, ADG, RGR, FCR and PI were numerically higher in male than in female rabbits, but ADFI was significantly (P<0.01) higher in males than in females (Table 1).

Table 1. Growth performance parameters of rabbits as affected by treatment and sex of rabbits.

Parameter	Experimental group			Sex of rabbit	
	G1	G2	G3	Male	Female
Initial LBW (g)	701.8±11.60	702.0±13.62	704.0±12.88	695.2±9.19	710.0±11.14
Final LBW (g)	1994.4±22.48	2137.5±47.02	2108.6±54.13	2109.3±36.95	2053.2±36.79
ADG (g/h/d)	23.07±0.51	25.63±0.91	25.03±0.91	25.26±0.678	23.92±0.676
RGR	95.77±1.801	100.69±2.309	99.23±1.955	100.58±1.599	96.56±1.739
ADFI (g/h/d)	87.01±1.01	85.34±1.20	84.54±1.04	86.99±0.90[a]	84.14±0.83[b]
FCR	3.79±0.08	3.41±0.13	3.45±0.14	3.52±0.10	3.58±0.10
VR	90	100	90	93.3	93.3
PI (%)	53.08±1.59[b]	65.61±4.23[a]	63.67±3.97[a]	62.53±3.19	59.27±2.84

a and b: Means denoted with different superscripts within the same row for each effect differ significantly at P<0.05. G1: control. G2: CoQ_{10}+propolis. G3: L-carnitine+propolis. LBW: Live body weight. ADG: Average daily gain: RGR: Relative growth rate. ADFI: Average daily feed intake. FCR: Feed conversion ratio. VR: Viability rate. PI: Performance index.

Effect of interaction:

Effect of interaction between treatment and rabbit sex on all growth performance parameters was not significant. This effect indicated the highest LBW (Fig. 1a), ADG (Fig. 1b) and RGR (Fig. 1c), reflecting the best FCR (Fig. 1d) and PI (Fig. 1e) with moderate ADFI (Fig. 1f) of male rabbits in G2 treated with a combination of CoQ_{10} plus PR.

Improving growth performance, in particular, PI of rabbits in treatment groups receiving PR in combination with CoQ_{10} or LC was mainly related to antioxidant properties of PR, CoQ_{10} and LC as documented by Seven et al. (2011), who mentioned that antioxidant compound is most important dietary supplementation.

Generally, each of treatment combination used in our study included an antioxidant property due to high content of polyphenoles such as flavonoids, terpenoids, tannins. Phenolic compounds have free-radical scavenging activity. In this line, many pharmacologic and biological properties (anti- bacterial, fungal, inflammatory, oxidant, viral and carcinogenic) of PR (Sabuncuoglu *et al.*, 2007), LC (Abdelrazik *et al.*, 2009) and CoQ10 (Hosseinzadeh *et al.*, 2015) were reported.

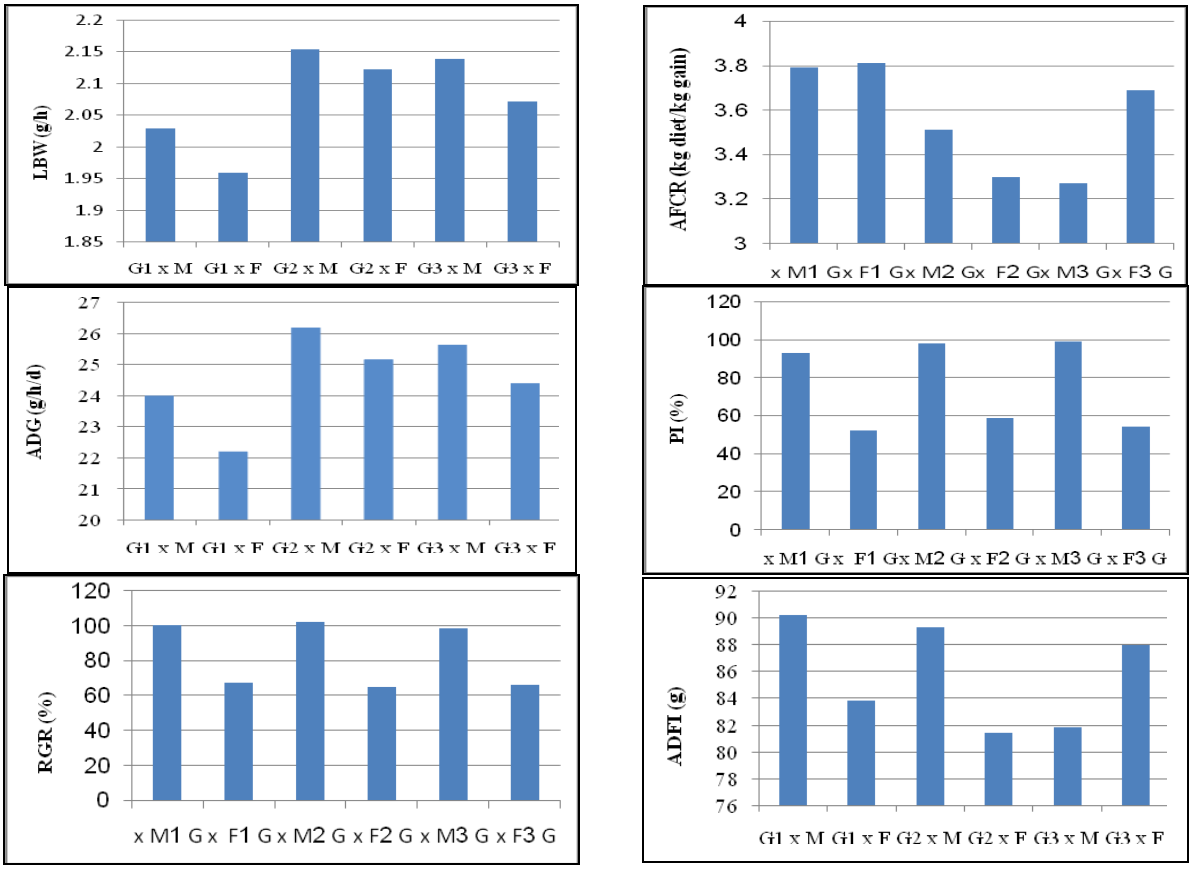

Fig. 1. Live body weight, LBW (a), average daily gain, ADG (b), relative growth rate, RGR (c), feed conversion ratio, FCR (d), performance index, PI (e) and average daily feed intake, ADFI (f) of male and female rabbits in different experimental groups.

It was suggested that PR stimulated the immunologic processes (Ansorge *et al.*, 2003) and has antibacterial (Nagaoku *et al.*, 2003), antifungal and antiviral (Güler *et al.*, 2003) as well as anticancer and anti-inflammatory (Blonska *et al.*, 2004) properties. Also, PR may show powerful local antibiotic and antifungal properties (Orsi *et al.*, 2005). In accordance with the present results, Gabr (2013) found similar trend of increase in LBW of rabbit bucks during treatment period with PR. Treatment with PR in both groups may be explained by stimulating effect of PR on mammalian tissue regeneration, as it enhanced protein biosynthesis

(Gabrys *et al*., 1986). In this respect, Seven (2008) reported that supplementation of PR (5 g/kg diet) was the most efficient treatment, and increased feed intake and improved digestibility of crude protein in laying hens. Seven *et al*. (2011) suggested that PR prevented oxidative stress in heat stressed broilers.

In addition, CoQ10 had a beneficial role in the cellular metabolism, cellular antioxidant and prevention of lipid peroxidation in mice (Hosseinzadeh et al., 2015). It serves as a coenzyme for several of the key enzymatic steps in the production of energy within the cell (Kapoor and Kapoor, 2013), and plays a key role in the mitochondrial electron transport chain and ATP synthesis (Abdulhasan et al., 2015). It protects the stability of the cell membrane, DNA from free radicals induced oxidative damage and helps recycling of vitamin E and maintain healthy energy levels (El‐Tohamy et al., 2012). Dietary supplementation with CoQ10 may increase mitochondrial activity within the cells (Bentov et al., 2010).

It was hypothesized more benefits from high energy pig diets supplemented with carnitine during the weaning period (Rincker *et al*., 2001). Improving PI of rabbits in G3 treated with LC in combination with PR is in coincidence with the recent results of Sherief (2014) who found significant improvement in LBW, weight gain and feed conversion of bulls treated with 2 g LC/h/d. Diet supplemented with LC improved feed conversion of pigs during weaning period (Weeden *et al*., 1990) or of grazing calves (White *et al*., 2001). Also, carnitine addition to complex nursery diets improved growth performance of early-weaned pigs (Owen *et al.*, 1996; Heo *et al*., 2000).

Concerning the effect of LC, the present results indicated a tendency of slight decrease in feed intake by rabbits in G3 as compared to control (G1), which disagreed with the results of Noseir *et al.* (2003) who found significantly greater intake (DM and TDN) from diet supplemented with LC during the 1st two postpartum months of multi-parous buffalo cows. Newton and Hayden (1989) found an increase in feed intake of weanling animals fed diet supplemented with LC. Sherief (2014) showed significant increase in feed intake (DM, TDN and DCP) of bulls orally treated with LC (2 g /h/d) as compared to the control bulls, while those the effect of LC at a level of 1 g was not significant. Therefore, the effect of LC on feed intake may associate with level of administration. LC also has a protective role against reactive oxygen species (ROS) by antioxidant properties (Agarwal and Said, 2004). On the other hand, LC with various protein sources decreased FCR in Holstein calves fed broiler litter. Also, Greenwood *et al*. (2001) found insignificant effect on average daily gain and feed conversion ratio of growing and finishing steers orally treated with of LC (2 g LC/d).

Liver function:

Morphology and blood parameters:

Effect of treatment was not significant on absolute and relative weight of the liver. Concentrations of total proteins and their fractions (albumin and globulin) or albumin to globulin ratio in blood serum were also not significantly affected by treatment. However, activity of AST and ALT showed marked reduction in serum of treated rabbits in G2 and G3, but the differences were significant (P<0.05) only for AST activity (Table 2).The present results in G2 and G3 indicated insignificant effect of treatments on serum protein fractions, reflecting no effect on protein metabolism of rabbits, in particular, albumin concentration. Generally, concentrations of protein metabolites are within a normal range as reported by Mitruka and Rawnsley (1977).

In agreement with the present results, albumin concentration was not affected by carnitine treatment in bulls (Sherief, 2014), lambs (Chapa *et al*., 1998) or cows (Carlson *et al*., 2007). However, Gabr (2013) showed that daily oral administration of rabbit bucks with 0.5 g PR/buck for 6 weeks significantly increased concentration of albumin and globulin, and consequently total proteins as compared to controls.

Table 2. Effect of treatment on liver morphology, and protein fractions and transaminases activity in blood serum of growing rabbits at the end of experiment (13 wk of age).

Liver function parameters	Experimental group G1	G2	G3
Liver morphology:			
Absolute liver weight (g)	56.51±5.31	55.73±2.78	58.86±4.44
Relative liver weight (%)	2.65±0.267	2.67±0.078	2.76±0.207
Protein fractions:			
Total protein (g/dl)	6.93±0.13	6.96±0.40	6.90±0.30
Albumin (g/dl)	4.01±0.17	4.05±0.06	3.82±0.24
globulin (g/dl)	2.92±0.04	2.91±0.37	3.07±0.06
Albumin/ globulin ratio	1.37	1.39	1.24
Activity of transaminases:			
AST (U/l)	58.33±3.66[a]	41.33±3.84[b]	42.00±2.08[b]
ALT (U/l)	71.00±12.76	52.00±6.42	65.66±11.72

a and b: Means denoted within the same row with different superscripts are significantly different at P<0.05.
G1: control. G2: CoQ_{10}+propolis. G3: L-carnitine+propolis.

However, concentration of proteins and their fractions were not significantly affected by increasing PR level up to double dose (1 g/buck), while albumin/globulin ratio in blood of rabbit bucks was not affected by PR administration. Also, Sherief (2014) reported that total proteins and globulin concentrations increased due to LC treatment. Also, Citil *et al.* (2009) observed an increased amount of albumin in blood samples of carnitine treated ewes.

As affected by PR, Giurgea *et al.* (1981) reported that daily administration of 20 mg/100 g LBW standard PR extract (SPE) to chicken for 15 days increased plasma total proteins, gamma-globulin contents and amino acids. In other studies, chicken fed SPE-diet showed a significant increase in serum total proteins (Giurgea *et al*., 1982) and muscle total protein (Giurgea *et al*., 1984) when compared to corresponding control. However in fishes (Rainbow Trout) fed diets containing 0, 0.5, 1.5, 4.5 and 9 g PR/kg diet for 8 weeks, Kashkooli *et al*. (2011) showed that all dosages induced no significant alterations in the levels of blood total protein, albumin and globulin when compared to the control group.

The present results and the previous findings indicated no deleterious effect of treatment on liver function of rabbits in treated groups.

Histological structure of liver:

The histological examination of liver samples taken from hepatic lobe of rabbits in all experimental groups revealed that hepatic lobule is consist of central hepatic vein within each lobule, and hepatocytes polyhedral in shape are arranged in radiated shape around each central hepatic vein allowed of blood sinusoid between them. It is of interest to note that rabbit in all groups showed normal architecture without septum between the hepatic lobules, indicating no marked effect of liver structure in all groups (Plate 1).

The magnification power at x100 revealed some histometric observations in liver of rabbits in each group as affected by treatment. In this line, the histological examination cleared that central hepatic vein was the widest, moderate and narrowest in G2, G1 and G3, respectively. Also, mild infiltration of monocytes in the central hepatic vein and bigger and darker nuclei within hepatocytes were observed in G2 and G3 than in G1 (control, Plate 2).

Based on these findings, slight improvement occurred in liver histology of G2 and G3 treated with combination of LC+PR or CoQ10+PR as compared to control (G1).Similar findings were observed by many authors on the effect of PR on liver histology. In this respect, El-Mahalaway *et al*. (2015) observed no histological changes in the control rats treated with 200 mg PR/kg as compared to that of the control group. Hepatitis group treated with PR showed preserved hepatic architecture as more or less normal hepatocytes, central vein and blood sinusoids.

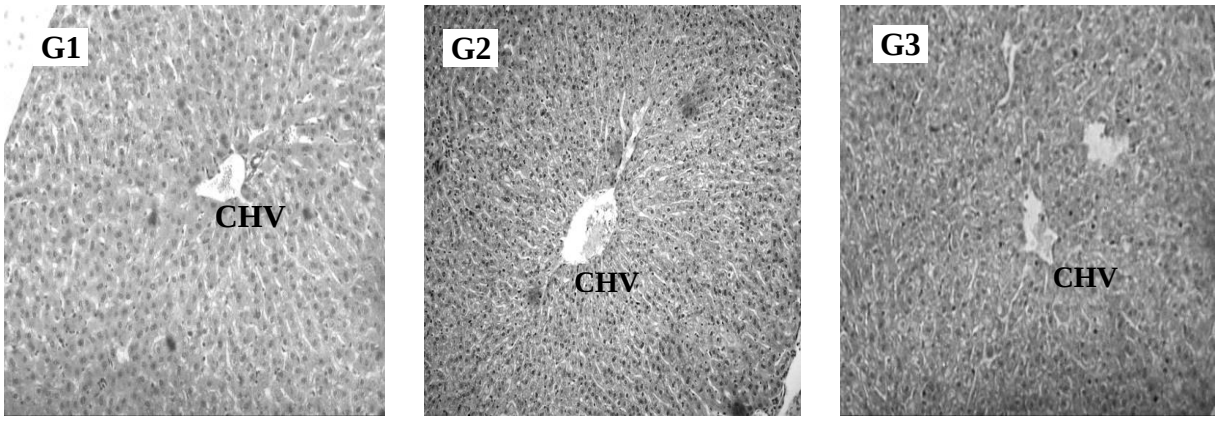

Plate 1. Section in liver of growing rabbits showing normal hepatic lobule, central hepatic vein (CHV) and radiated hepatocytes in G1, G2 and G3. (H & E stain, x 100)

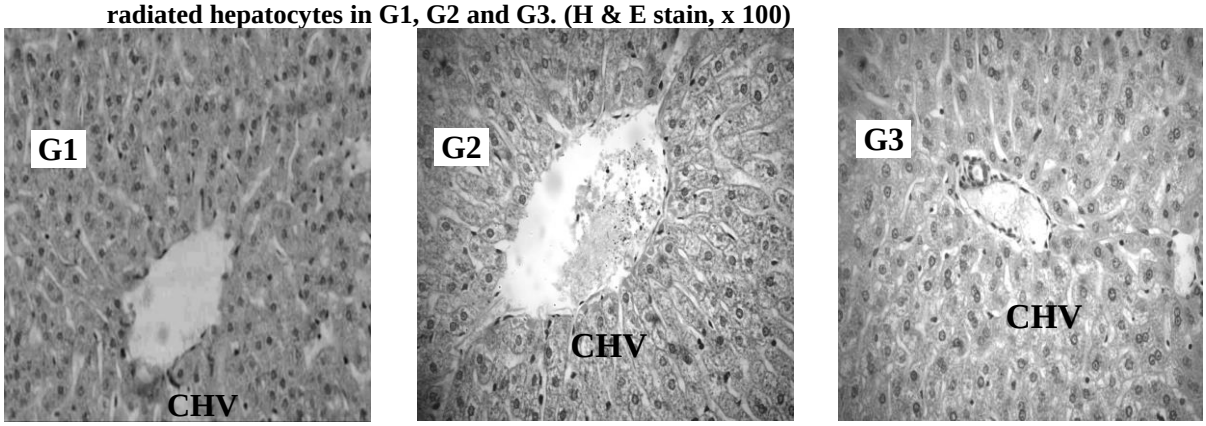

Plate 2. Magnification in the previous sections revealed CHV, polyhedral in shape and radiated arrangement of hepatocytes, and blood sinusoids in G1, G2 and G3.(H & E stain, x 400)

Also, Nassar *et al*. (2013) found that ethanolic PR extract injected S/C alone or with formalized inactivated *P. multocida* vaccine improved liver function. However, in diabetic mice treated with water PR extract, half of the samples were similar to control, however the hepatocytes were less vacuolized, but not significantly. In the other half of the samples histological image was quite different. Sinusoids were dilatated and hepatocytes around central veins were swollen but not vacuolized (Oršolić *et al*., 2012). On the other hand, Tarry-Adkins *et al*. (2016) reported that recuperated offspring showed greater ($P<0.001$) collagen deposition in liver than did control and CoQ10 supplementation prevented this effect of maternal diet. Generally, similar observations were observed by Gad and Zaghloul (2013) in liver of rate treated with GT extract as antioxidant.

Kidney function:

Weight and protein metabolites:

Effect of treatment on absolute and relative kidney weight was not significant. Concentrations of creatinine and urea in blood serum were also not significantly affected by treatment (Table 3). These results indicated that combination of CoQ10 or LC with PR had no significant effect on serum protein metabolites, reflecting normal kidney function of rabbits in G2 and G3. In accordance with the present results, insignificant difference in urea-N was reported by Rincker *et al*. (2003) in weanling pigs fed LC

supplemented diet. However, other authors (Citil *et al*., 2009) observed a reduction in serum urea level in ewes fed diet supplemented with LC (500 mg/kg).

Histological structure of kidney:

The histological examination of kidney samples taken from the renal cortex of rabbits in all experimental groups cleared intact renal cortex containing normal Malpigian corpuscles and convoluted renal tubules. Malpigian corpuscles were denser and renal tubules were rounded in G2 as compared to less density of Malpigian corpuscles and oval renal tubules in G1 and G3 (Plate 3).

Table 3. Effect of treatment on kidney morphology, and protein metabolites in blood serum of growing rabbits at the end of experiment (13 wk of age).

Parameter	Experimental group		
	G1	G2	G3
Kidney morphology:			
Absolute kidney weight (g)	14.08±1.24	12.32±0.44	11.66±0.86
Relative kidney weight (%)	0.66±0.05	0.57±0.01	0.55±0.03
Protein metabolites:			
Creatinine (mg/dl)	1.52±0.13	1.46±0.06	1.58±0.07
Urea (mg/dl)	41.00±3.51	37.66±0.88	41.33±2.02

G1: control. G2: CoQ_{10}+propolis. G3: L-carnitine+propolis.

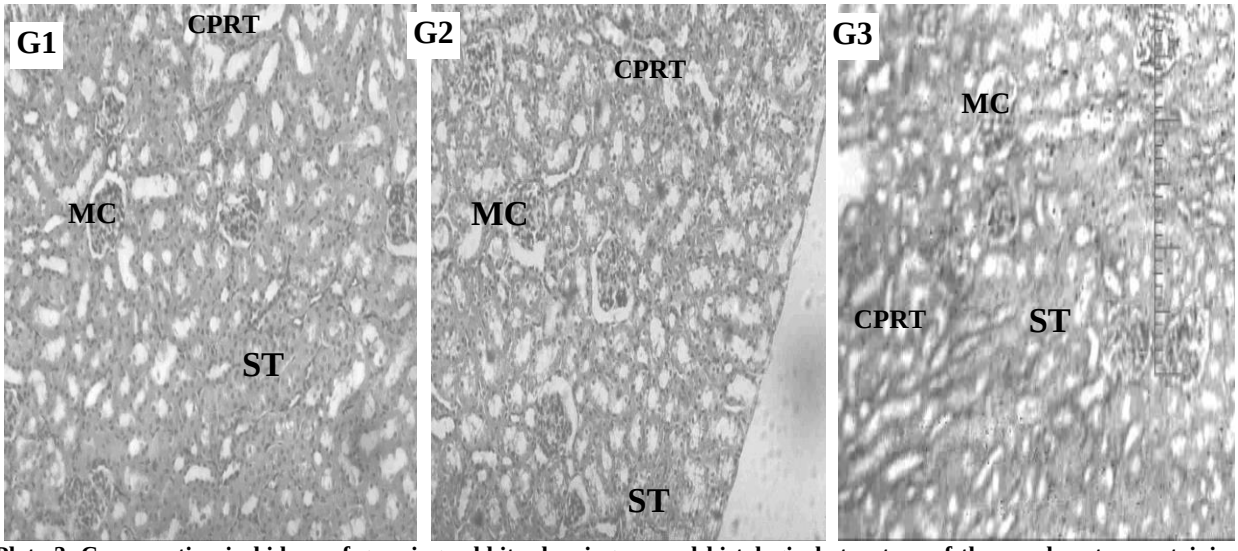

Plate 3. Cross-section in kidney of growing rabbits showing normal histological structure of the renal cortex containing Malpigian corpuscles (MC), convoluted proximal renal tubules (CPRT) and stroma (ST) in G1, G2 and G3. (H & E stain, x 100)

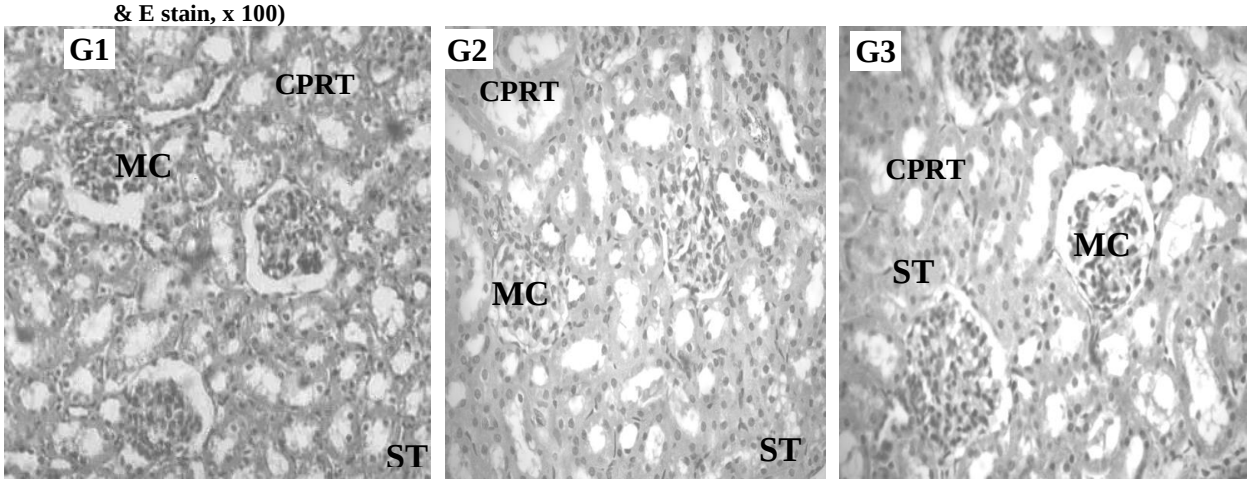

Plate 4. Magnification in the previous sections revealed Bowman's capsule and capillaries within MC as well as epithelial single layer of renal tubules walls in G1, G2 and G3. (H & E stain, x 400)

The magnification power at x100 revealed slight differences in Bowman's capsule space off Malpigian corpuscles, being wider in G3 than in G1 and G2, but renal tubules had nearly similar structure in all groups, lining with single cubical epithelial cells (Plate 4).

These findings may indicate intact histological architecture of kidney in rabbits of treated groups (G2 and G3) as compared to control one (G1).The present examination in rabbits is in agreement with the results of El-Sheikh *et al*. (2012), who revealed that, control and CoQ10 groups had normal structure of renal glomeruli and cortical tubules in rats. Also, they found that concomitant administration of CoQ10 in the low dose with Doxorubicin-Induced Nephrotoxicity (DIN) in rats resulted in reversal of histopathological damage induced by DIN, with regeneration of renal epithelial cells lining of cortical tubules and restoration of normal morphology to renal cortex.

In association with the effect of PR on the histological structure of rabbit kidney in G2 and G3, Oršolić *et al*. (2012) observed that kidneys of diabetic mice treated with water PR extract showed similar changes to control diabetic mice but with much larger lymphocyte infiltrations and more dilated tubules in the

outer cortex. In rabbits, Nassar *et al*. (2013) also found that ethanolic PR extract injection improved general health conditions, kidney functions in addition to reduction of the severity of adverse clinical signs and mortality rates.

Thyroid hormones:

Effect of treatment on thyroid function, in terms of T3 and T4 concentrations in blood serum of rabbits was not significant, although there was a tendency of higher concentrations of T3 and T4 in blood serum of rabbits in G2 as compared to those in G1 and G3 (Table 4). These results indicated that treatments had not significant effect on metabolic hormones of the thyroid gland, reflecting normal thyroid function of rabbits in treated groups. Despite these results, Ansorge *et al.* (2003) suggested that PR has an anabolic effect, which is in similar trend with increasing T3 and T4 in G2 andG3 treated with PR.

Table 4. Effect of treatment on concentration of T3 and T4 in blood serum of growing rabbits at the end of experiment (13 wk of age).

Parameter	Experimental group		
	G1	G2	G3
Thyroid hormones:			
T3(ng/ml)	1.01±0.04	1.11±0.06	1.03±0.07
T4(µg/dl)	2.37±0.127	2.88±0.136	2.84±0.217

G1: control. G2: CoQ_{10}+propolis. G3: L-carnitine+propolis.

Lipid metabolism:

Fat weight:

Average weight of abdominal fat significantly ($P<0.05$) decreased in G2 and G3 compared with G1, while effect of treatment on subcutaneous fat or absolute or relative weight of total fat was not significant (Table 5). Such results may indicate remarkable effect of treatments on fat distribution, not reducing body fat, within the rabbit body as affected by CoQ10 and LC in combination with the effect of PR.

Table 5. Effect of treatment on carcass fat weight and lipid metabolism of growing rabbits at the end of experiment (13 wk of age).

Item	Experimental group		
	G1	G2	G3
Carcass fate weight:			
Abdominal fat weight (g/h)	19.88±1.88[a]	11.36±1.17[b]	10.66±2.08[b]
Subcutaneous fat (g)	11.65±1.40	13.01±4.16	15.40±1.18
Total fat weight (g/h)	31.53±2.35	24.37±3.34	26.07±3.27
Relative total fat weight (%)	1.47±0.085	1.17±0.161	1.22±0.151
Lipid metabolites in blood serum:			
Total cholesterol (mg/dl)	125.00±14.01	109.66±2.33	135.33±12.87
HDL (mg/dl)	49.80±2.10	58.26±2.77	61.90±3.59
LDL (mg/dl)	55.26±13.42	31.80±2.15	41.40±9.01
Triglycerides (mg/dl)	99.66±7.12	98.00±2.64	109.00±10.69

a and b: Means denoted within the same row with different superscripts are significantly different at P<0.05.

G1: control. G2: CoQ_{10}+propolis. G3: L-carnitine+propolis.

In accordance with the obtained results on rabbits, LC supplementation was reported to reduce carcass fat (Weeden *et al*., 1990), lipid accretion (Owen *et al*., 1996) and back fat thickness (Owen *et al.,* 2001) in weaning pigs.LC had dual effects by enhancing mitochondrial lipid metabolism. The ATP is synthesized by β-oxidation of fatty acids within mitochondria, which requires carnitine (Dunning *et al.,* 2010, 2011). Mitochondria play a key role in the physiology of eukaryotic cells during all stages of life and their main function is to provide cells with ATP through oxidative phosphorylation (Cummins, 2004; Smith *et al.,* 2005). Mitochondrial dysfunction may lead to incomplete detoxification of the free radicals, which may lead to oxidative damage to macromolecules such as lipids, proteins, and DNA (Abdelrazik *et al.,* 2009).

Lipid profile:

In association with the results of fat weights, concentrations of total cholesterol, HDL, LDL and triglycerides were not statistically affected by treatments, although there was a tendency of total cholesterol, LDL and triglycerides concentrations to be lower in G2 treated with CoQ10 and PR than in other groups (Table 5). Treatment of LC affect lipid metabolism (Heo *et al*., 2000) by decreasing tissue lipid content (Chen *et al.,* 2008). This reduction was associated with transfer of acyl groups across the mitochondrial membranes to stimulate lipid metabolism through (Owen *et al*., 1996). However, the present results contrasted those reported by Sherief (2014) on bulls and suckled ewes (Citil *et al*., 2009). In addition, CoQ10 had a beneficial role in the cellular metabolism, cellular antioxidant and prevention of lipid peroxidation in mice (Hosseinzadeh *et al*., 2015).

Economic feed efficiency:

As expected, total cost of feeding during the experimental period was higher for treatment groups (G2 and G3) than in control (G1) by 31 and 25%, respectively. This result was related to cost of treatment because rabbits in all groups showed nearly similar feed intake. According these differences, net revenue showed an opposite trend to total cost, being higher in G1 than in G2 and G3.Based on increasing viability rate and PI in G2 and increasing PI in G3 as compared to G1. Also, economic feed efficiency (EFE) and relative EFE were the highest in G2, moderate in G3 and the lowest in G1 (Table 6).

Table 6. Effect of treatment on economical efficiency of growing rabbits in different experimental groups.

Item	G1	G2	G3
Total feed intake (kg/h)	4.87	4.78	4.73
Cost of feeding (L.E./h)	12.18	11.95	11.84
Cost of oral treatment (L.E./h)	-	1.44	0.81
Cost of dietary treatment (L.E./h)	-	2.67	2.67
Total cost (L.E./h)	12.18	16.06	15.32
Total weight gain (kg/h)	1.29	1.44	1.40
Total revenue (L.E./h)	28.38	31.68	30.80
Net revenue/h	16.20	15.62	15.48
Viability rate (VR)	90	100	90
Performance index (PI, %)	53.08	65.61	63.67
Economic feed efficiency (EFE)*	7.74	10.24	8.87
Relative economic efficiency (%)	100	132	114

G1: control. G2: CoQ_{10}+propolis. G3: L-carnitine+propolis.

Price of each kg feed intake and kg gain was 2.5 and 22.0 L.E., respectively according to market prices at 2016.Total revenue= Total weight gain x price of each kg gain.Net revenue= Total revenue - total cost.

*** Economic efficiency= Net revenue x viability rate x performance index.**

CONCLUSION

In light on the foregoing results, treatment of growing rabbits during marketing period (5-13 wk of age) with propolis in combination with coenzyme Q10 or L-carnitine twice/week led to functional liver and kidney with normal lipid profile. These findings were associated with remarkable improvement in growth performance parameters.

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الأداء الإنتاجي، وظائف الكبد والكلية، التمثيل الغذائي للدهون وهرمونات الغدة الدرقية للأرانب النامية المعاملة بأنواع مختلفة من العوامل التمثيلية

محمد الفاتح حماد[١] , جمال عاشور[٢] , شريف عبد الونيس جبر[١] , جورج عزت يونان[٣] و دعاء عبد العاطى كامل[١]

[١] قسم الإنتاج الحيواني - كلية الزراعة - جامعة طنطا – مصر.

[٢] قسم الإنتاج الحيواني - كلية الزراعة - جامعة القاهرة –مصر.

[٣] معهد بحوث الإنتاج الحيواني - مركز البحوث الزراعية - دقي – جيزة – مصر.

تهدف الدراسة الحالية إلى تقييم تأثير المعاملة عن طريق الفم مرتين أسبوعيا بالكارنيتين الحر أو المساعد الأنزيمي كيو١٠ (CoQ10) على أداء النمو - وظيفة الكبد والكلية - هرمونات الغدة الدرقية والكفاءة الاقتصادية للغذاء للأرانب النامية المغذاة على عليقه محتويه على بروبوليس. تم تقسيم ٦٠ من الأرانب المفطومة حديثا (النيوزيلاندى الأبيض- ٥ أسبوع من العمر و٧٠٢.٥٨ ± ١٢.٧٠ جم) إلى ٣ مجموعات متماثلة (٢٠ في كل منهما، ١٠ من الذكور و١٠ من الإناث). تم تغذية الأرانب في المجموعة الأولى عليقه تجارية مكعبه بدون أي معاملات، وكانت بمثابة المجموعة الضابطة. تم تغذية الأرانب في المجموعات الثانية والثالثة علي نفس عليقه المجموعة الأولى مضاف اليها ٠.٥ جرام بروبوليس/كجم وعوملت بالتجريع عن طريق الفم ب١٠ ملجم CoQ10/كجم من وزن الجسم أو ٤٠ ملجم كارنيتين/كجم من وزن الجسم على التوالي. وتحتوى العليقة على 18٪ CP، 13٪ CF و٢٨٠٠ كيلو كالورى/كجم عليقه. تمت تغذيه الأرانب في كل المجموعات علي عليقه لحد الشبع وتوافر الماء في الحلمات في كل الأقفاص. كانت المعاملة بالخليط مرتين أسبوعيا من عمر ٥ إلي ١٣ أسبوع للأرانب. تم تسجيل وزن الجسم الحي والغذاء المأكول وحساب متوسط الزيادة اليومية والكفاءة التحويلية الغذاء والنسبة المؤية للحيوية ومعدل النمو النسبي ودليل أداء النمو. في نهاية التجربة (١٣ أسبوع من العمر)، تم أخذ عينات دم من ثلاثة ذكور أرانب مذبوحة من كل مجموعة لتقدير تركيز البروتينات الكلية والألبيومين والكرياتينين واليوريا والكولسترول والبروتينات الدهنيه مرتفعه الكثافة والبروتينات الدهنيه منخفضة الكثافة والدهون الثلاثية ونشاط الأنزيمات الناقلة لمجموعة الأمين (ALT، AST) وتركيز هرمونات الغدة الدرقية (T3, T4). تم تسجيل وزن الكبد والكلى والدهن الجسم. تم أخذ عينات صغيرة من أنسجة الكبد والكلى لفحص التركيب النسيجي. أوضحت النتائج عدم وجود تأثير معنوي للمعاملات علي كل من وزن الجسم النهائي ومتوسط الزيادة اليومية والغذاء المأكول ومعدل النمو النسبي والكفاءة التحويلية للغذاء ولكن هذه القياسات كانت أكثر ارتفاعا في المجموعة الثانية ومتوسطة في المجموعة الثالثة وأقلهم في المجموعة الأولي ومرتفعة في الذكور عن الإناث. لم يوجد تأثير معنوي فى قياسات الأداء الإنتاجي على التداخل بين المعاملة وجنس الأرانب في كل المجموعات. لا يوجد زيادة معنوية في الوزن المطلق والنسبي للكبد والكلية وتركيزات البروتينات الكليه والألبيومين والجلوبيولين والكرياتينين واليوريا والكولسترول والبروتينات الدهنيه مرتفعه ومنخفضة الكثافة والدهون الثلاثية وهرمونات الغدة الدرقية (T3, T4) وكذلك نسبة الالبيومين إلي الجلوبيولين ونشاط الأنزيم الناقل لمجموعة الأمين (ALT) في سيرم الدم بينما انخفض معنويا نشاط الأنزيم الناقل لمجموعة الأمين (AST) في المجموعتين الثانية والثالثة عن المجموعة الأولي. لم يلاحظ حدوث أي تغييرات في التركيب النسيجي للكبد والكلى. كان متوسط وزن الدهون في منطقة البطن اقل معنويا في المجموعتين الثانية والثالثة عن المجموعة الأولي، في حين أن الوزن المطلق أو النسبي لدهون تحت الجلد لم يختلف معنويا. الخلاصة: أدت معاملة الأرانب النامية خلال فترة التسويق من ٥ إلى ١٣ أسبوع من العمر بخليط من البروبليس وأي من الكارنيتين الحر أو المساعد الأنزيمي كيو١٠(CoQ10) مرتين / أسبوع إلى وظيفية طبيعيه لكل من الكبد والكلى مع مظهر طبيعي للدهون في الدم. وصوحبت النتائج السابقة بتحسن ملحوظ في خصائص الأداء الإنتاجي للأرانب.