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COMPARATIVE STUDIES ON REPRODUCTIVE MALE RABBITS AS AFFECTED BY THERAPEUTIC OF IVERMECTIN OR BOTH OF GARLIC AND CINNAMON OILS TREATMENTS. b. BIOCHEMICAL BLOOD, HORMONES AND SEMEN CHARACTERISTICS IN MALE RABBIT

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Thirty-six V-line male rabbits ten months age, average weight 3.5 kg were used. They were allocated randomly into six equal groups. First and second were served as a negative (NC) and positive (PC) control. Third group was injected by double dose (1mg/kg body weight) of ivermectin (IV) via subcutaneous injection, fourth, fifth and sixth groups were treated with 5% garlic oil (GO), 5% cinnamon oil (CO) and 5% garlic oil + 5% cinnamon oil mixture (MO), respectively. Rabbits were treated GO, CO and MO received daily topically treatment for 7 successive days. Groups PC and IV were treated with paraffin oil and ivermectin. Blood samples were collected at 1, 7 and 14 days of treatment to biochemical analysis. Semen characteristics and reaction time (libido) were recorded.

Results showed that *there were a significant (P≤0.05) decreased in total protein, albumin, globulin, testosterone, semen characteristics, TAC in rabbits infested groups compared with NC group. But there were a significant (P≤0.05) increase in ALT, AST, creatinine, urea and uric acid, cortisol, T_3 and T_4, MAD in the rabbits infested groups compared with NC group. Rabbits treated with ivermectin recorded a significant (P≤0.05) decrease at 1 and 7 days in serum total protein, albumin compared with other groups, while, globulin decreased gradually from day 1, 7 and 14 comparable with other groups. Serum total protein, albumin, ALT, AST, creatinine, urea and uric acid were increased toward to NC group at 7^{th} and 14^{th} days of therapeutic.*

Garlic and cinnamon oils caused a decrease in ALT, AST, creatinine, urea and uric acid with time compared with PC and IV groups. While, injected ivermectin for infested rabbits led to significant (P≤0.05) increase in cortisol, T_3 and T_4 hormones at 1^{th}, 7^{th} and 14^{th}

days. Likewise, testosterone significant (P≤0.05) increased at 7th and 14th day's similarity therapeutic by oil treated groups. Also, they recorded a significant (P≤0.05) decreasing at 14 days in MAD and significant (P≤0.05) increasing in TAC compared with other groups. Semen volume, sperm concentration, advanced motility and live sperm% were significantly decreased (P≤0.05) of infested rabbits compared with NC group, while abnormal sperm% increased. In the same context, the semen characteristics were significant increased in all therapeutic groups at 7th and 14th toward the NC group.

Conclusively, *five percent of garlic or cinnamon oil is so effective in treating rabbits injured by Sarcoptec scabei compared to ivermectin with no side effects on liver and kidney functions or semen characteristics.*

Key words: Sarcoptec Scabei, Ivermectin, Cinnamomum zeylanicum, Allium sativum oils, Hematology Biochemistry, Antioxidant enzymes, hormones, semen quality.

Sarcoptes scabiei is a burrowing mite that inhabits the epidermis of the skin causing sarcoptic mange in mammals and it's a highly contagious parasite (Walton and Currie, 2007). *Sarcoptes scabiei* is an important rabbit ectoparasite because of the possibility of zoonotic infection and considerable losses in weight, productivity, wool, and fiber quality (Harrenstien *et al.*, 1995). In such conditions, animals affected with *Sarcoptes scabiei* may affected by other health problems such as dermatitis, pyoderma, sometimes eczema and urticarial. Several constraints such as resistance of *Sarcoptes scabiei* to synthetic medicaments due to the repeated use of the same mode of action drugs in infected animals. Side effects of medicaments, the long residual properties of most of the synthetic drugs available in the use justify the cause to find alternative approaches to control *Sarcoptes scabiei* mite (Khan *et al.*, 2012). Mahmoud *et al.*, (2014) mentioned that the severely infested rabbits exhibited significantly reduced total white blood cell, lymphocyte, and eosinophil counts. Animals are infested with skin infection mange cussed disturbed the oxidant/antioxidant balance by mites and some oxidative substances would be constantly generated in animals (Singh *et al.*, 2012). In addition, the immune status of the animal, the nutritional status and oxidative stress may play very important roles in the pathogenesis of this

disease (Singh *et al*., 2011). When these substances generated overloaded the antioxidant defense, the free radicals could interact with endogenous macromolecules, alter the cellular functions, and induce some serious adverse effects on the skin, including edema, erythema, wrinkling, inflammation and autoimmune reaction (Muthukumaran *et al*., 2008).

The levels of malonyldialdehyde (MAD) in the infested rabbits were markedly increased, and this was associated with the deterioration of cells, the development of skin lesions and the clinical manifestation of mange (Kanbur *et al*., 2008). Sarasa *et al*. (2011) reported that the sarcoptic mange was associated with reduced size-corrected testes mass in Iberian ibex which supports the hypothesis that parasitism is a determining factor in gonad in plasticity in male mammals.

Therefore, the present study was designed to investigate the role of ivermectin, garlic and cinnamon oils against *Sarcoptic scabiei* and their effects on hematology, biochemistry, antioxidant enzymes, hormones and semen quality.

MATERIALS AND METHODS

Experimental animals:

Thirty-six V-line male rabbits ten months age weighting about 3.5 kg were used for the present study. They were housed in clean, separate and wire-floored metal cages and maintained under standard laboratory conditions. The ambient temperature was 25±2°C with 55-64% relative humidity and a 16 h light and 8 h dark. They were allowed to a standard pellet diet (17% crude protein, 2.56% crude fat and 2500 Kcal/kg-ration digested energy and 12.5% crude fiber). Food and water were available *ad libitum*. Rabbits were kept under the same environmental conditions during the experimental period (30 days).

Experimental design: Rabbits were allocated into six equal groups each contain 6 males as follow:

Group 1: It was served as a negative control (non-infested and non-treated) (NC).

Group 2: It was served as positive control (infested and non-treated) (PC)

Group3: Infested rabbits were served as therapeutic group and treated with ivermectin injection by double therapeutic dose 1 mg kg^{-1} of ivermectin via subcutaneous injection (IV) (Atakisi *et al.,* 2009).

Group 4: Infested rabbits were served as therapeutic group and treated with 5% garlic oil *(Allium sativum)* in paraffin oil (GO).

Group 5: Infested rabbits were served as therapeutic group and treated with 5% cinnamon oil *(Cinnamomum zeylanicum)* in paraffin oil (CO).

Group 6: Infested rabbits were served as therapeutic group and treated with mix of garlic and cinnamon oils, (5% garlic oil + cinnamon oil 5%) in paraffin oil (MO).

Groups treated with GO, CO and MO received daily topically treatment embrocating by 2.5 ml of therapeutic oil for 7 successive days. PC and IV groups were treated locally with paraffin oil and double therapeutic dose ivermectin by injection 1 mg kg^{-1} of ivermectin, respectively.

Treatments on the infested areas in limbs and pinna of rabbits were done after cleaning with worm water and remove of scabs according to Fichi *et al.,* (2007a). Rabbits in all groups were followed up by skin scaping and examination under stereomicroscope till complete recovery.

Essential oils:

The essential oils used in this study were provided by the medicinal and aromatic plants division belonging to Research Institute, Agricultural Research Center in Egypt. The chemical analysis of essential oils was done with a GC - ULTRA gas chromatograph according to Adams (2007).

Biochemical Analysis:

All blood samples of 3 mL were collected from the ear vein at times immediately before injection of ivermectin as control and on 1, 7 and 14 days after treatment. Blood samples were centrifuged at 3000 r.p.m. for 20 min to separate a clear serum. Collected serum samples were subjected to biochemical analysis of urea and creatinine (Henry, 1974), alanine aminotransferase (ALT), aspartate aminotransferase (AST) activities (Reitman and Frankel, 1957), total protein (Sonnenwirth and Jarett, 1980), creatinine (Henry, 1974), albumin (Doumas, 1971), globulin was calculated, malonyaldehyde (MAD) and total antioxidant capacity (TAC) (Ippoushi *et al*., 2005). All biochemical parameters were analyzed by commercially available kit methods. GNW-Model: SM-721Spectrophotometers, Absorbance Microplate Reader and other laboratory equipment aids were used for biochemical analysis. Moreover, each parameter was done according to the instructions of its kit.

Serum testosterone concentration was determined using RIA method according to Wilke and Utley (1987). Triiodothyronine (T_3), thyroxin (T_4)

and cortisol hormones determination were done according to Abdel-Fattah *et al.,* (2011) using radioimmunoassay (RIA) technique.

Semen Quality:

Advanced sperm motility from at least three fields was examined at 37 ºC under a phase microscope at 40× and assessed from 0 to 100%. A weak eosin solution was used at a rate of 1:99 before counting the cells, for evaluation of sperm concentration ($\times 10^6$/ml) as to Smith and Mayer (1955) by the hemocytometer slide. The percentage of live spermatozoa was determined by using stains that penetrate cells with damaged membranes. The total number of motile sperm was calculated by multiplying percentage of motile sperm by total sperm outputs. (Correa and Zavos, 1996).

Reaction time (libido):

A matured cyclic doe (teaser) was introduced to the buck every 2 weeks interval to monitor their sex drive. In this study, reaction time was considered as an indication of libido. The time in seconds it took for the rabbit bucks to sniff, groom and mount the female was recorded with a stop watch, and libido scored using the scoring pattern of 1-5 (no libido - high libido) as described by (Chibundu, 2005).

Statistical analysis:

All data were subjected to analysis of variance according to the statistical analysis system (SAS, 2002). The differences among groups means were tested by using Duncan's multiple rang test (Duncan, 1955).

RESULTS AND DISCUSSION

Chemical composition of the essential oils:

Gas chromatography analysis of garlic and cinnamon oils is cited by El-Speiy *et al.,* (2016a).

Biochemical serum blood analysis:

Concerning biochemical serum blood analysis at 14 day's post treatment, Figure (1) showed a significant ($P \leq 0.05$) decreased in blood serum total protein, albumin and globulin in PC compared with NC group. While, treated rabbits with ivermectin recorded a significant ($P \leq 0.05$) decrease (at day 1and 7) in serum total protein and albumin when compared with other groups.

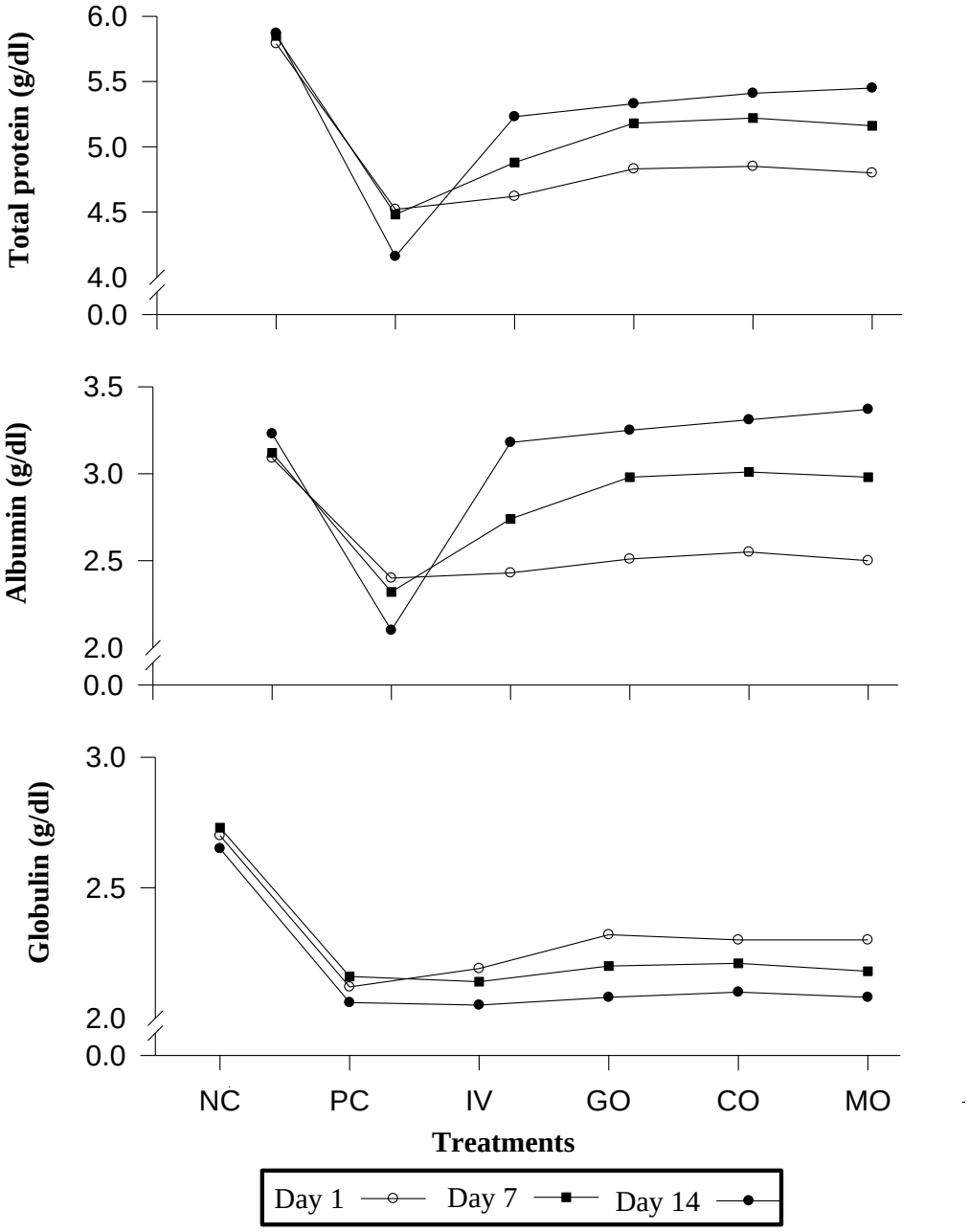

Figure 1: Effect of ivermectin, garlic and cinnamon oils on total protein, albumin and globulin levels of male rabbits.

Serum globulin decreased gradually from day 1, 7 and 14 comparable with other groups. However, serum total protein and albumin increased toward values of NC group at 7^{th} and 14^{th} days of treatment. But globulin was significantly ($P \leq 0.05$) decreased in its level compared with NC group.

There are many factors which can affect the level of albumin circulating in the blood. Chronic liver disease causes decrease in the amount of albumin produced, and consequently, the level of albumin in the blood is reduced. Albumin is also part of most automated chemistry screening panels (Canadian liver foundation, 2015). Albumin is a major protein which is formed by the liver (Gines and Arroyo, 2000). Albumin is the major extracellular source of thiols. Albumin can also limit the production of reactive oxidative species by binding free copper, an ion known to be particularly important in accelerating the production of free radicals (Quinlan *et al*., 1998). This study revealed that oils treated groups showed significant difference ($P \leq 0.05$) in serum total protein, albumin and globulin when compared with NC group. These results were in agreement with those obtained for rabbits (Seddiek *et al.,* 2013). On the other hand, rabbits in PC group showed a significant decreased in serum total protein, albumin, and globulin when compared with the corresponding values of other groups. Atakisi *et al.*, (2009) suggested that ivermectin did not alter protein and albumin parameters during therapeutic course. Emtenan *et al.*, (2010) mentioned that rabbits treated with cinnamon oil and infested with sarcoptes showed elevation of protein, albumin and globulin when compared with positive control group. Tollba and Hassan (2003) stated that garlic treatment led to an increase in the gamma globulin production from plasma cells. Mohamed *et al.*, (2016) mentioned that garlic extract supplementation increased blood serum total protein and globulin on growing lambs. Jenkins (2000) and Meredith and Rayment (2000) stated that liver inflammation and necrosis (such as that caused by parasites) is responsible for making albumins; therefore, decreases in serum albumin levels (Figure 1).

Regarding biochemical analysis 14 day's post treatment, results showed a significant ($P \leq 0.05$) increase in serum blood ALT, AST, creatinine, urea and uric acid in the PC group compared with NC group. Treated rabbits with ivermectin recorded a significant ($P \leq 0.05$) increased at 1, 7 and 14 days in ALT, AST enzymes, creatinine, urea and uric acid compared with other groups (Figures 2 and 3). On the other hand, treated rabbits with oils showed significant ($P \leq 0.05$) decrease in ALT, AST, creatinine, urea and uric acid

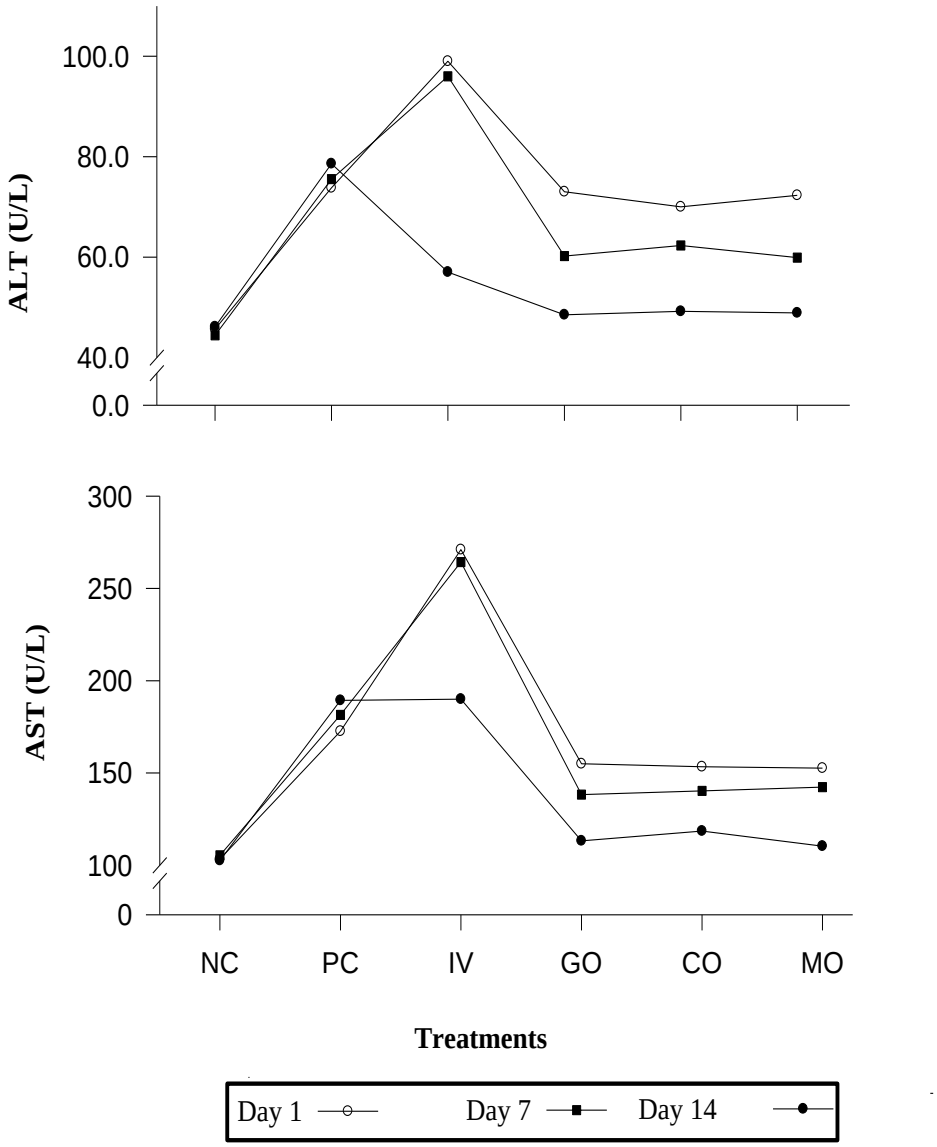

Figure2: Effect of ivermectin, garlic and cinnamon oils on serum ALT and AST levels of male rabbits.

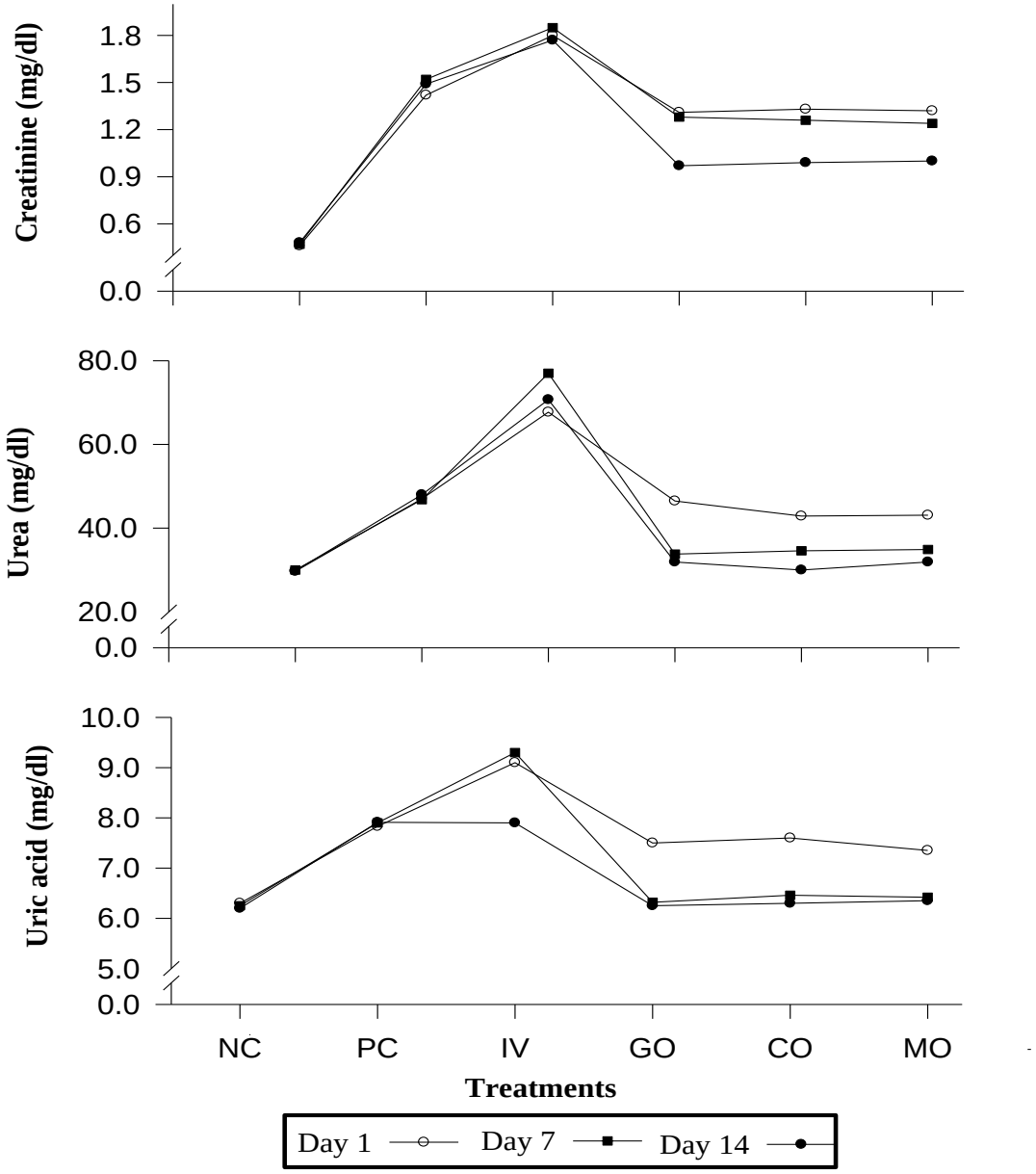

Figure 3: Effect of ivermectin, garlic and cinnamon oils on serum creatinine, urea and uric acid levels of male rabbits.

compared with PC group and IV group. In the same context data illustrated that treatment with oils decreased ALT, AST, creatinine, urea and uric acid with time compared with PC and IV groups during the experiment (Figure 2).

Liver enzymes (ALT and AST) are commonly measured clinically as a part of a diagnostic evaluation of hepatocellular injury to determine liver health (Wang *et al*., 2012). Alanine aminotransferase this enzyme is of limited use for rabbit liver disease, if ALT is significantly elevated, it may indicate liver inflammation and necrosis (such as that caused by parasites, and or hepatic lipidosis) (Jenkins, 2000).

The positive control rabbits showed a significant increase in serum ALT and AST levels. This may be attributed to the ear tissues damage induced by mite's infestation and its toxic excretory products. Such results were in agreement with those mentioned for rabbits (Seddiek *et al.,* 2013 and Mahmoud *et al.,* 2014). Biochemical analysis indicated that the levels of ALT and AST in rabbits significantly ($P \leq 0.05$) increased in rabbits in PC and IV. Such results indicated an adverse effect of ivermectin on the liver and results were in agreement with those mentioned for macrocyclic lactones for the treatment of rabbits (Eman and Abdella, 2000). Liver function was negatively affected, which was monitored by increasing ALT and AST after ivermectin injection in rabbits (Eman and Abdella, 2000). Serum ALT, AST, urea, and creatinine levels were significantly ($P \leq 0.05$) increased after 28 days of treatment with ivermectin in swine and cattle (Slantna *et al.*, 1989). The toxic effects of ivermectin on liver and kidney functions were transient, and the treated rabbits required not less than 3 months after injection of ivermectin to regain their normality (Eman and Abdella, 2000), in same context Arise and Malomo (2009) confirmed a significant increase in both enzyme activities for IV group with highest increments indicating the incidence of hepatic injuries due to ivermectin medication. Also, Ashang (2009) showed the effects on some liver function enzymes such as ALT and AST in ivermectin treated in Wistar Albino rats. The findings of raised enzymes following ivermectin administration, suggest that, in liver disease, the use of ivermectin must be done with caution (Hutchinson *et al*., 2009). Transient non-significant renal disturbances were observed which suggested that ivermectin seem to cause minor damage to the glomeruli (Arise and Malomo, 2009). Reduced renal blood flow associated with high serum urea concentration may impair the secretory function of the kidney. Malfunction in the glomerular filtration results in retention of substances including urea,

uric acid and creatinine and this might be responsible for their high serum levels in the treated groups (Selvakumar *et al*., 2013).

Treatment with garlic oil reduced serum ALT and AST enzymes, creatinine, urea and uric acid towards the normal levels on the day 14 post treatment (Figures 2 and 3). This is may be due to the acaricidal effect of garlic oil. On the other hand, the obtained results disagreed with the findings of Ibrahim *et al.*, (2000) on rabbits. The harmony in our results showed non-significant changes of creatinine in all treated rabbits except that treated with ivermectin which showed a significant ($P \leq 0.05$) increase (Figure 3). These results indicated that the garlic extract has no harmful effect on kidney functions. The obtained results endorsed the results of El-Shater *et al.*, (1998) on rats. Emtenan *et al.*, (2010) mentioned that therapeutic infested rabbits with cinnamon oil (1.25%) showed normal liver and kidney functions. Saber *et al.*, (2014) indicated that treating animals with cinnamon led to improvement in the histological structure of the kidney and ameliorative effect against damage.

Concerning biochemical serum blood analysis during treatment, showed the regulates significant ($P \leq 0.05$) decrease in serum testosterone, but increase in cortisol, T_3 and T_4 hormones in the PC compared with NC group, respectively (Figures 4 and 5). While, injected ivermectin for infested rabbits led to significant ($P \leq 0.05$) increase in cortisol, T_3 and T_4 hormones at 1^{th}, 7^{th} and 14^{th} days. Likewise, testosterone was significantly ($P \leq 0.05$) increased at 7^{th} and 14^{th} day's similar to treatment by oil. Clearly, at day 14^{th} the concentrations of testosterone, cortisol and T_4 hormones comparable between NC and all oil groups (Figures 4 and 5).

Testosterone is a steroid hormone from the androgen group in mammals, reptiles, birds and other vertebrates. In mammals; testosterone is primarily secreted in the testicles of males and the ovaries of females, although small amounts are also secreted by the adrenal glands (Vodo *et al*., 2013).

Parasitism by (*Sarcoptes scabiei*) is known to affect the social behavior of hosts in host-pathogen systems (Hughes *et al.*, 2004). Testis size is intimately associated with testosterone dynamics (Toledano-Díaz *et al.*, 2007), and testosterone is predictive of a male's rank trajectory (Beehner *et al*., 2006), of likeliness to initiate aggressions (Virgin and Sapolsky, 1997) and of outcome of male–male interactions (Bergman *et al*., 2006). Thus, through testosterone, a relationship between testes size and behavior is highly plausible. Free testosterone is the serum testosterone that is not bound to sex hormone

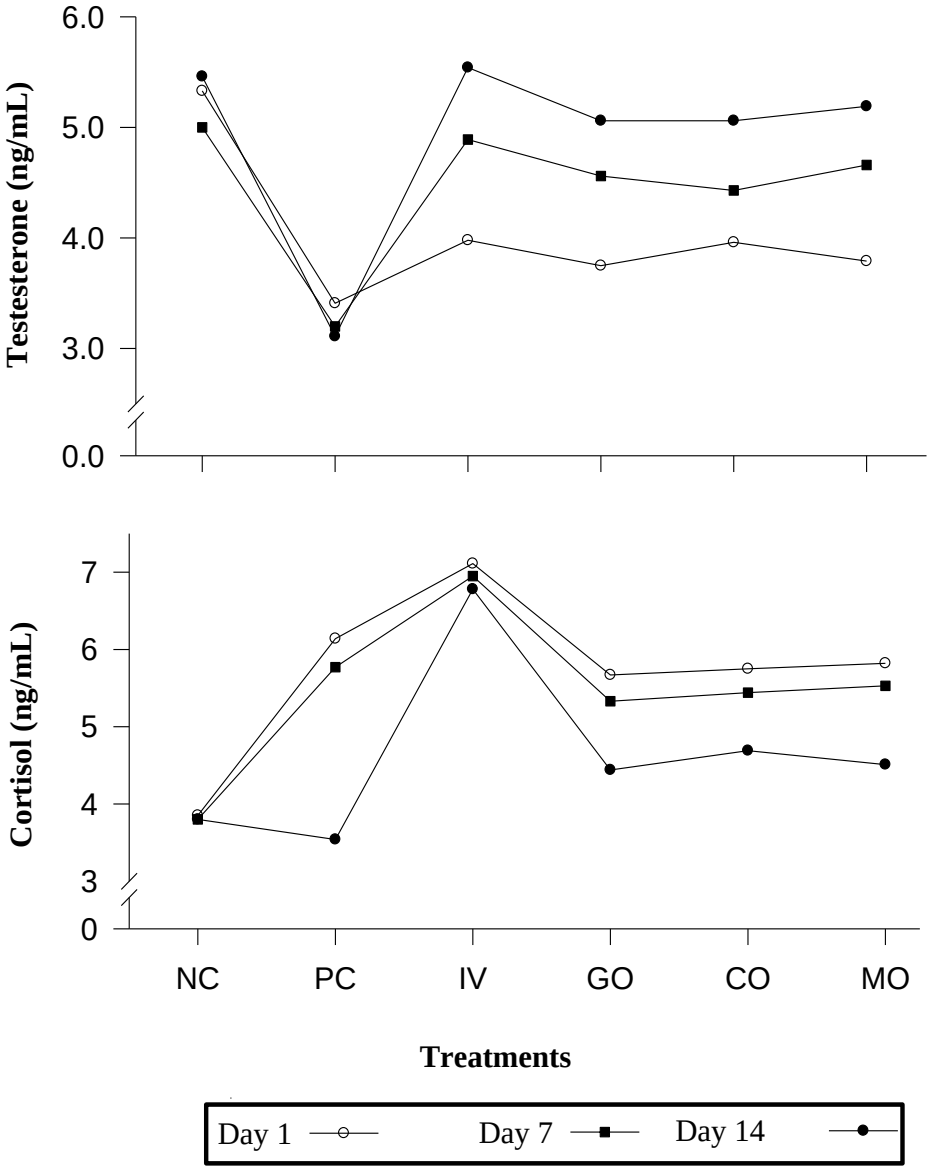

Figure 4: Effect of ivermectin, garlic and cinnamon oils on serum testesterone and cortisol levels of male rabbits.

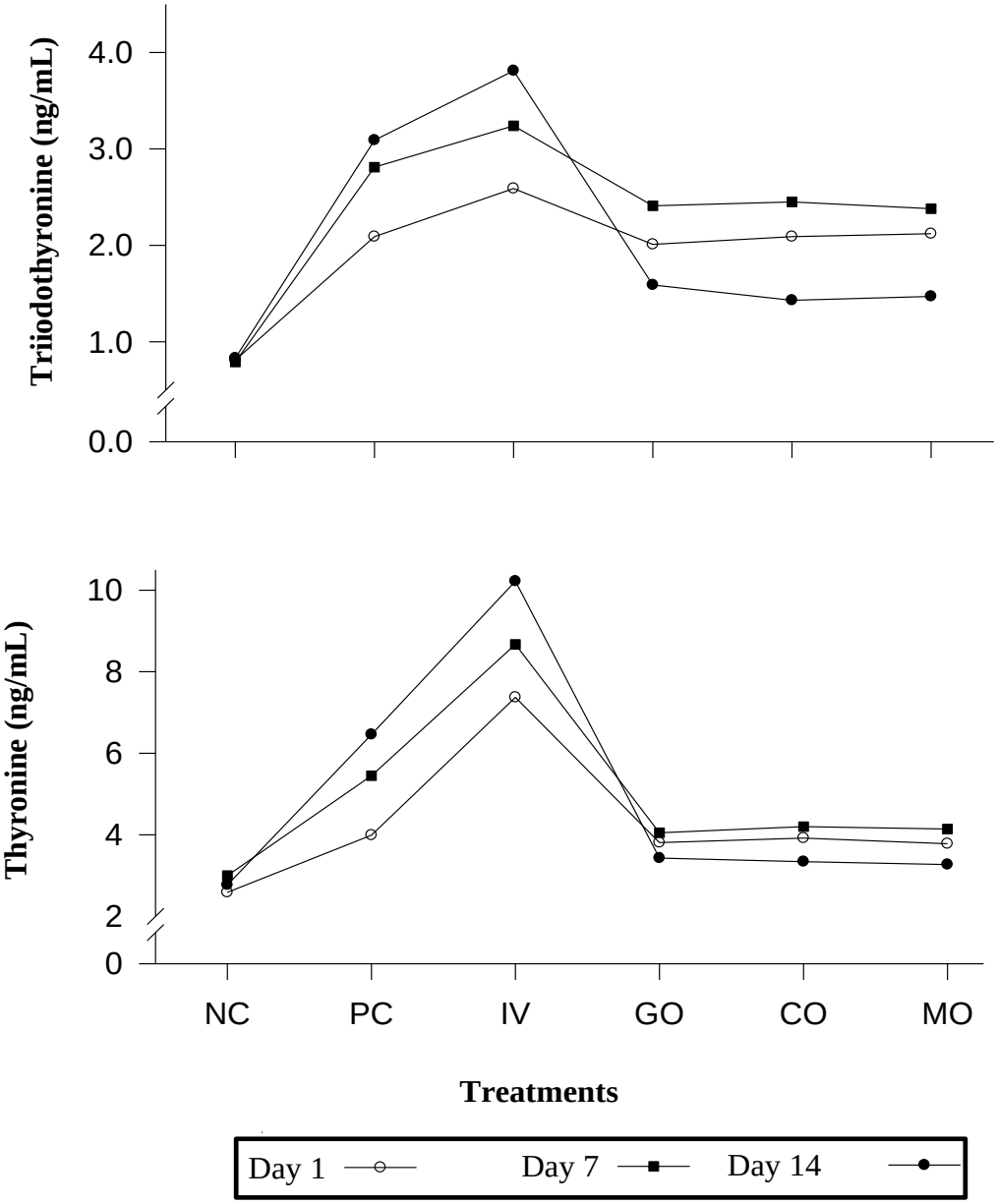

Figure 5: Effect of ivermectin, garlic and cinnamon oils on serum triiodothyronine (ng/mL) and thyronine (ng/mL) levels of male rabbits.

binding globulin (SHBG) or albumin. It is free testosterone that is biologically active able to exert its effect by permeating a cell and activating its receptor (Kevin *et al*., 2012). The obtained data in Figure 3 revealed a significant increase in testosterone and free testosterone in IV and oils treated groups with a high increase in IV group that improve the male reproduction. Kadry *et al*., (2015) showed that ivermectin caused unobservable changes in serum testosterone and sex hormones binding globulin. Yuriko *et al.*, (2001) suggested that dietary supplementation with garlic altered hormones associated with protein anabolism by increasing testicular testosterone in rats.

Cortisol is a steroid hormone produced by the zona fasciculata of the adrenal cortex and it is released in response to stress although it acts to restore homeostasis, prolonged secretion of cortisol, which may be due to excessive secretion or chronic stress, leads to major physiological changes, suppressing immune and reproductive functions (Muehlenbein and Watts, 2010). It is observed a trend towards an increase in serum cortisol levels in chronically infested animals. Serum cortisol is often used in stress and welfare assessments (Orihuela *et al*., 2009). However, it is important to consider that the nature of the aversive stimulus leads to major physiological changes. With respect to external parasites, serum cortisol levels have been related to tick deleterious in cattle. Tick deleterious also affected various characteristics of growth and metabolism in growing cattle (Garris *et al*.,1991), and serum cortisol levels also have been directly associated with intestinal parasite abundance in helminthic infestations (Kyriazakis and Day., 1998). Increasing level of cortisol in ivermectin treated rabbits is a clear indication of the stress condition of those animals (Marieb and Hoehn, 2010).

Physiological activities of free thyroid hormones depend on thyroxine-binding globulin (TBG), thyroxine-binding pre-albumin (TBPA) and albumin plasma concentrations. In acute Protein Energy Malnutrition (infestation status), free T_4 levels may be either normal or high. After acute decreasing in thyroid hormone binding proteins, free T_4 levels increased but when malnutrition prolonged free T_4 levels decreased. For this reason it was reported that free T_4 levels were important in explaining thyroid functions in children with PEM (Tibaldi and Surks, 1985).

Furthermore, the circulatory levels of T_3 and T_4 hormones have been found to play an important role in correlating the persistent infection as well as subclinical condition of infection (David *et al*., 1998). Similarly, in stressful animals, an increase in plasma cortisol concentration causes an

alteration of neutrophil function and an increase in susceptibility to infection (Roth and Kaeberle, 1982).

The treatment with garlic extract has been shown to stimulate the release of cytokines such as IL-2, IFN-α, IFN-γ an increase in the natural killer activity and enhance phagocytic activity of peritoneal macrophages (Kyo *et al*., 1998). The therapeutic efficacy of garlic for its cytotoxic, antitumor, antifungal, antibacterial, antiviral and antiprotozoal properties showed that it was used traditionally since long time is thought to be caused by an organic sulphur compound 'Ajoene' (4,5,9 –trithiadodeca 1,6, 11-triene-9-oxide) (Ledezma and Apitz, 1998). Further, garlic is also reported to contain selenium, vitamins A, B, C and E (Williamson, 2002).

Oxidant serum blood analyses:

Concerning biochemical analysis 14 day's post treatment, it was seen significant ($P \leq 0.05$) increase in MAD and significant decrease in TAC in PC and IV groups compared with NC group (Figure 6). On the contrary, treated rabbit with oils recorded significant ($P \leq 0.05$) decrease in MAD at 14 days and significant ($P \leq 0.05$) increase in TAC compared with other groups (Figure 6).

Regarding to oxidative stress induced by ivermectin injection a significant decrease in serum TAC levels were recorded in a positive relationship to the periods of experimental in IV group. On the contrary, the levels of MAD were significantly ($P \leq 0.05$) increased in treated group. In regard to oxidative stress, there was a significant increase in MAD and significant decrease in glutathione, glutathione peroxidase, glutathione-Stransferase, superoxide dismutase, catalase and serum ascorbate in infested groups (Mahmoud *et al*., 2014). In agreement with our result, significant decrease in TAC of V-line rabbits injected by ivermectin was observed by (Atakisi *et al*., 2009). Ivermectin may produce free radicals and thus results in cytotoxic effect on the parasite. Ivermectin was reported to counteract against scabies agents by inducing free radicals associated damage and by decreasing antioxidant enzyme activity (Behera *et al*., 2011). These findings may suggest that ivermectin is a safe anti-parasitic drug for mammals but to less extent; it may have an effect on the balance between oxidants and antioxidants (El-Shenawy, 2010)

Carmia Borek, (2001) mentioned that the garlic extracts treated animals showed significantly decrease ($P \leq 0.05$) MAD as compared with PC and IV groups because the garlic extracts elicit antioxidant action by scavenging reactive oxygen species, enhancing the cellular antioxidant enzyme (e.g.

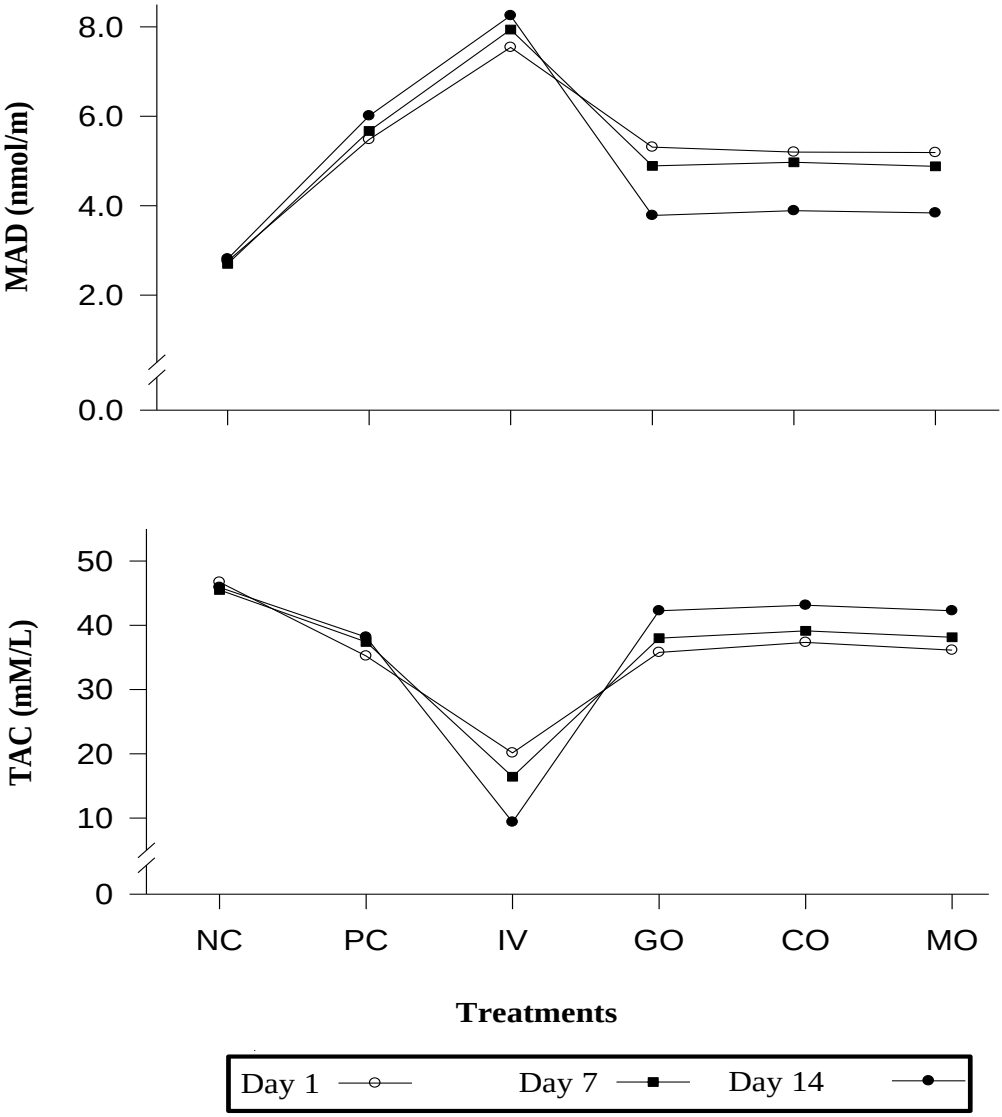

Figure 6: Effect of ivermectin, garlic and cinnamon oils on serum MAD and TAC levels of male rabbits.

superoxide dismutase, catalase and glutathione peroxidase) and increasing glutathione in the cells. Ide *et al*., (1996) reported that garlic and its major organo sulfur constituents had a scavenging effect on hydrogen peroxide, and inhibited the chain of oxidation induced by a hydrophilic radical initiation.

Moreover, the essential cinnamon oil mechanism depended on constituents approximately 20-26 compounds to effect on cellular antimicrobial. As typical lipophilia, they pass through the cell wall and cytoplasmic membrane and disrupt the structure of their different layers of poly saccharides, fatty acid and phospholipid and permeabilizethem (Carson *et al.*, 2002). Cytotoxicity appears to include such membrane damage. In bacteria, the permeabilization of the membranes is associated with loss of ion and reduction of membranes potential, collapse of the proton pump and depletion of the ATP pool (Turina *et al.*, 2006). Moreover, it was evident that essential oil could coagulate the cytoplasm (Gustatson *et al.*, 1998) and damage lipid and proteins (Burt, 2004).

Semen quality:

Data presented in Table 1 showed significant decrease ($P \leq 0.05$) in semen characteristics (volume, concentration, motility, live sperm and abnormal spermatozoa) and increase in reaction time of PC group compared with NC group. In the same context, the semen characteristics were significantly ($P \leq 0.05$) increased in all treated groups at 7^{th} and 14^{th} toward the NC levels.

Obtained data in previous figures indicated a significant decrease ($P \leq 0.05$) in testosterone, TAC and increase in cortisol, T_3, T_4 and MAD in serum blood infested male rabbits with *Sarcoptic Scabies.*

Nabila *et al.,* (2013) mentioned that *sarcoptic* mange is associated with reduced size-corrected testes mass in Iberian ibex which supports the hypothesis that parasitism is a determining factor in gonad plasticity in male mammals. Santiago-Moreno *et al.,* (2010) examined the relationship between sperm quality and the level of parasitism in infested Iberian ibex and looked separately for linear relationships. Testis size is intimately associated to testosterone dynamics (Toledano-Díaz *et al.,* 2007), and testosterone is predictive of a male's rank trajectory (Beehner *et al.,* 2006). Consequently, reduced testes mass in mange individual may not only threaten reproductive success through sperm competition (Preston *et al.,* 2003), but may also, severely hinder the recruitment, the courtship and eventually the mating success of infested hosts.

Table (1): Effect of therapeutics by ivermectin, garlic, cinnamon, and combination of them on semen characteristics and reaction time of male rabbits.

Groups	Volume (ml)	Sperm Concentration (10^6/mL)	Motility (%)	Live Sperm (%)	Abnormal Sperm (%)	Reaction Time (sec)
Negative control (NC)						
1st day	0.71±0.017^{Aa}	389 ± 31.9^{Aa}	82.4 ± 1.12^{Aa}	86.8 ±3.56^{Aa}	15.2 ± 0.45^{Ba}	31.7 ± 1.21^{Ba}
7th day	0.69±0.015^{Aa}	401 ± 22.7^{Aa}	83.1 ± 1.98^{Aa}	85.1 ±4.24^{Aa}	14.9 ± 0.52^{Ba}	30.8 ± 1.34^{Ba}
14th day	0.72±0.013^{Aa}	425 ± 30.1^{Aa}	80.9 ± 1.75^{Aa}	86.2 ±3.10^{Aa}	16.1 ± 0.63^{Ba}	32.1 ± 1.02^{Aa}
Positive control (PC)						
1st day	0.42±0.016^{Ba}	219 ± 17.5^{Ba}	60.7 ± 1.09^{Ba}	72.7 ±1.45^{Ba}	22.1 ±0.48^{Ab}	35.7 ± 0.96^{ABa}
7th day	0.36±0.021^{Ca}	207 ± 22.8^{Ca}	60.4 ± 2.50^{Ca}	71.2 ±1.20^{Ba}	25.2 ±1.01^{Aab}	33.1 ± 1.04^{ABab}
14th day	0.31±0.012^{Ba}	202 ± 19.1^{Ca}	60.1 ± 2.06^{Ba}	69.7 ±1.44^{Ba}	26.3 ±0.99^{Aa}	30.1 ± 1.11^{Ab}
Ivermectin 1% (IV)						
1st day	0.49±0.017^{Bb}	243 ± 18.5^{Bb}	68.7 ± 3.21^{Bb}	75.4 ± 0.95^{Bb}	17.2 ± 0.73^{Ba}	35.7 ± 1.19^{Aa}
7th day	0.56±0.019^{ABab}	368 ± 25.2^{ABa}	78.6 ± 2.25^{ABab}	80.7 ± 1.05^{Aab}	15.3 ± 0.82^{Ba}	33.1 ± 0.97^{ABab}
14th day	0.69±0.020^{Aa}	397 ± 27.4^{Aa}	80.4 ± 3.11^{Aa}	82.8 ± 1.11^{Aa}	14.6 ± 0.99^{Ba}	30.1 ± 1.07^{Ab}
Garlic oil (GO)						
1st day	0.47±0.028^{Bb}	241 ±20.4^{Bb}	67.8 ±2.08^{Bb}	73.9 ± 1.31^{Bb}	18.1 ± 0.73^{Ba}	36.2 ± 1.25^{Aa}
7th day	0.53±0.039^{Bb}	355 ±27.5^{Ba}	75.8 ±1.97^{Bab}	82.1 ± 1.23^{Aa}	15.6 ± 0.49^{Ba}	34.1 ± 1.34^{ABa}
14th day	0.66±0.030^{Aa}	391 ±28.5^{Aa}	80.4 ±3.11^{Aa}	80.7 ± 1.25^{Aab}	15.4 ± 0.91^{Ba}	32.3 ± 1.10^{Aa}
Cinnamon oil (CO)						
1st day	0.46±0.018^{Bb}	239 ±20.4^{Bb}	66.9 ±2.21^{Bb}	75.3 ± 1.01^{Bb}	17.9 ± 0.83^{Ba}	37.1 ± 1.55^{Aa}
7th day	0.51±0.019^{Bb}	357 ±28.5^{Ba}	75.1 ±1.95^{Bab}	79.6 ± 0.93^{Aab}	16.1 ± 0.69^{Ba}	35.2 ± 1.74^{ABab}
14th day	0.64±0.020^{Aa}	388 ±32.2^{Aa}	80.4 ±2.51^{Aa}	83.1 ± 1.05^{Aa}	15.7 ± 0.97^{Ba}	33.8 ± 1.60^{Ab}
Mixture of (garlic + cinnamon) oils (MO)						
1st day	0.45±0.025^{Bb}	236 ±17.4^{Bb}	65.8 ±1.81^{Bb}	70.8 ± 1.31^{Bb}	17.4 ± 0.63^{Ba}	37.1 ± 0.85^{Aa}
7th day	0.54±0.029^{Bb}	364 ±22.5A^{Ba}	74.9 ±2.05^{Bab}	80.5 ± 1.33^{Aa}	16.7 ± 0.79^{Ba}	35.2 ± 1.04^{ABab}
14th day	0.65±0.025^{Aa}	378 ±24.5^{Ba}	79.5 ±2.71^{Aa}	82.4 ± 1.45^{Aa}	15.6 ± 0.91^{Ba}	32.8 ± 11.04^{Ab}

Means within the same column carrying different small letters are significantly different at (P≤0.05),
Means within the same column under each parameter carrying different capital letters are significantly different at (P≤0.05). Values are expressed as Lsmeans ±SE;

Barth and Bowman (1994) detected that low testosterone may interfere with the same cellular metabolic processes, leading to similar outcomes in defects of the cells affected during spermatid metamorphosis

Correlation coefficients between seminal hormonal levels and physical semen parameters in male rabbits showed that the level of T_3, T_4 and testosterone had significant positive correlations with good semen characteristics (ejaculate volume, sperm motility, sperm cell concentrations, total number of sperms output and number of motile sperms per ejaculate) and had significant negative correlations with bad semen characteristics (high in each of reaction time, dead sperm%, sperm abnormality% and acrosomal

abnormality%). In rats rendered thyrotoxic by T_4 resulted in decreased serum gonadotropin levels (Schneider *et al*., 1979), decrease in total lipids, cholesterol, and phospholipids in testes, and synthesize increased amounts of testosterone (Aruldhas, *et al*., 1986). However, T_3 also plays a significant role in differentiation of the seminiferous epithelium, and studies in rodents have shown that T_3 is an important factor in maturation of Leydig cells. The presence of T_3 is necessary to initiate differentiation of mesenchymal cells into Leydig progenitor cells, and T_3 works in concert with other hormones [luteinizing hormone (LH) and IGF-I] to promote Leydig cell development (Mendis-Handagama and Ariyaratne, 2001). Also it was suggested that T_3 is a component of the neuroendocrine system that regulates seasonal cycles of reproductive activity (Dutta *et al*., 2013). On the other hand, cortisol shows the opposite finding with T_3, T_4 and testosterone. Cortisol levels had significant negative correlations with good semen characteristics and significant positive correlations with bad semen characteristics. Therefore, the level of any one of these hormones could be used in detection of semen quality to predict the reproductive performance of male rabbits under different conditions and lighting**.**

Agarwal *et al*., (2005) mentioned that the oxidative damage caused by free radicals was a major cause of idiopathic oligospermia and even had adverse effects on sperm structure and produces sperm abnormalities (Coskun *et al*., 2005). There are two antioxidant systems in the human body (antioxidant defense system), containing proteins such as albumin and ceruloplasmin which bind to metal ions and prevent the formation of active species, and thus, prevent a chain reaction of reactive oxygen species. While scanning the system, antioxidants like vitamin E, vitamin C, glutathione peroxidase, eliminate produced ROS in order to inhibit plasma membrane lipid peroxidation.

Harmony with current work, Onakpa, *et al.,* (2010) indicated dramatic changes in semen parameters represented by significant decrease in the sperm count as well as increase in the sperm abnormalities followed ivermectin injection. The deleterious effect of ivermectin on sperm could be due to the oxidant nature of certain neurotransmitter metabolites which triggered by ivermectin (Shoeb, 2013). Additionally, treatment with ivermectin lead to lack of spermatogenesis stimulating hormone (SSH) resulting in decrease in sperm concentration and lack of active testosterone, consequently, increase in sperm abnormalities occurred which varies from abnormalities in head as enlarged

head, abnormal middle piece and abnormal tail, which may be coiled, bent tail (Onakpa, *et al*., 2010). Moreover, Low levels of sperms concentration after ivermectin injection may be due to effect of ivermectin in a dose dependent manner on muscle fiber of male reproductive system leading to decrease in the total force of ejaculation (Burg et *al*., 1979). Accordingly, this ensures a persistence harmful effect of ivermectin on the reproductive organs function. However, Orgebin Crist *et al*., (1976) mentioned that the composition of the epididymis fluid may be affected the mechanism necessary for sperm maturation, transport and storage. On the other hand, Rabab *et al.,* (2015) recorded the treatment of bulls with ivermectin improved the semen quality, total sperm output ejaculate and the activity of acid and alkaline phosphatases of seminal plasma.

Garlic contains a wide variety of phytochemicals and microcomponents such as trace elements, vitamins, fructans, flavonoids, and sulphur compounds, which can effectively scavenge free radicals (Khaki *et al*., 2011). Oi *et al*., (2001) demonstrated that the increased concentration of testicular testosterone after feeding rats with 8 g of garlic powder was due to an increase in luteinizing hormone (LH) level in plasma. Indeed, crude garlic and garlic powder may have the same active compounds (Oi *et al*., 2001). Ola-Mudathir *et al*., (2008) indicated that aqueous extracts of garlic caused an increase in the catalase activity and protect the testis and spermatozoa against cadmium toxicity.

Hammami *et al*., (2008) found that rats fed with 10%, 15% or 30% *Allium sativum* (AS) containing diet, showed a significant increase in the number of empty seminiferous tubules in testes and a decrease in the level of testosterone. Male rats fed with crude garlic showed damaged testicular function and spermatogenesis. Also, a decreased prostate weight was associated with a reduction in citric acid content in rats fed with 30% garlic.

Cinnamomum (family of Lauraceae) species contain volatile oils, tannins, terpenoids, mucilage, oxalates and starch. Different chemical constituents of C.zeylanicumare known to have significant germicidal, antiulcerogenic and cytotoxic effects. Shah *et al.,* (1998) demonstrated that the extract of cinnamomum increased the weight of testes, caudae epididymidies and seminal vesicles in the treated male mice, indicating a possible stimulation of hormonal levels in the animals. Also, the sperm count and motility of the treated animals were significantly higher than the control group.

Ranasinghe *et al.,* (2013) mentioned that *C. zeylanicum* has 65.3% antioxidant activity and also a very strong free radical scavenging activity.

According to *in-vivo* and *in-vitro* studies, *C .zeylanicum* has antimicrobial, antiparasitic, antioxidant and free radical scavenging properties. Furthermore, it could lower serum cholesterol, blood pressure and blood glucose in diabetic people. Khaki *et al*., (2010) showed that using 75 mg/kg of C. zeylanicum as an antioxidant in food increased SOD, GPX, and CAT, leading to the elimination of ROS and elevation of testosterone secretion; it could enhance its fertility properties.

Finley, Arash Khaki (2015) demonstrated that the GPX, CAT and SOD contained by *C. zeylanicum* could increase serum antioxidant levels male rats. Therefore, it has the potential to restore fertility and normal spermatogenesis, sperm quality parameters, and to improve testosterone level and sperm quality parameters, such as population, viability and motility, while in the meantime decreasing the MAD level.

Conclusively, from these results, it could be concluded that five percent of garlic or cinnamon oil is so effective in treating rabbits injured by *Sarcoptec scabei* compared to ivermectin with no side effects on liver and kidney functions or semen characteristics.

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مقارنة تأثير المعاملة بالإيفرمكتين وزيت الثوم أو زيت القرفة على الكفاءة التناسلية لذكور الأرانب

ب - تقدير بعض مكونات الدم، مستوى الهرمونات، صفات السائل المنوى.

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إستخدم فى هذة التجربة عدد ٣٦ ذكر أرنب عمر ١٠ شهور بمتوسط وزن ٣,٥ كيلو جرام من خط V-Line، حيث تم توزيعهم عشوائيا إلى ٦ مجاميع تجريبية كالتالى :

المجموعه الأولى : كنترول سالب (بدون عدوى بدون معاملة).

المجموعه الثانية : كنترول موجب (تم عمل عدوى بدون معاملة).

المجموعة الثالثة : تم عمل عدوى وتم الحقن تحت الجلد بجرعة ١مجم/كجم وزن حى من عقار إيفرمكتين ١% بجرعتين بينهما ١٤ يوم.

المجموعة الرابعة: تم عمل عدوى وتم معاملة الأرانب موضعيا بزيت الثوم ٥% لمدة ٧ أيام متصله.

المجموعة الخامسة: تم عمل عدوى وتم معاملة الأرانب موضعيا بزيت القرفة ٥% لمدة ٧ أيام متصله.

المجموعة السادسة: تم عمل عدوى وتم معاملة الأرانب موضعيا بخليط من زيت الثوم ٥% + زيت القرفة ٥% فى لمدة ٧ أيام متصله.

وتم سحب عينات دم فى اليوم ١، ٧، ١٤ من المعاملة وتم عزل السيرم وذلك لإجراء تحليل البروتين الكلى، الألبيومين، ووظائف الكلى (كرياتينين، يوريا، حامض بوليك) ووظائف الكبد (ALT, AST) ومضادات الأكسدة (MAD, TAC) وهرمونات الدرقية (T_3, T_4) وهرمون الذكورة (التستستيرون) وهرمون الإجهاد (الكورتيزول).

كما تم فحص وتقدير صفات السائل المنوى (حجم القذفة، الحركة التقدمية، تركيز الحيوانات المنوية، ونسبة الحيوانات المنوية الحية، عدد الحيوانات المنوية المتحركة، وجملة الحيوانات المنوية المنتجة) ، كما تم تقدير زمن إستجابة الذكور.

وقد أوضحت النتائج مايلى:

- حدث إنخفاض معنوى عند مستوى (٥%) فى كل من مكونات سيرم الدم (البروتين الكلى، الألبيومين، الجلوبيولين، هرمون التستستيرون) وصفات السائل المنوى المدروسة ومضادات الأكسدة الكلية TAC فى الأرانب المصابة بطفيل الجرب مقارنة بالمجموعة الضابطة السالبه (NC).
- حدث إرتفاع معنوى عند مستوى (٥%) فى كل من إنزيمات الكبد (ALT, AST) ووظائف الكلية (كرياتينين، يوريا، حامض البوليك) وهرمونات الكورتيزول، T_3, T_4 ومضادات الأكسدة بالدم MAD فى الأرانب المصابة بطفيل الجرب مقارنة بالمجموعة الضابطة السالبه (NC).
- سجلت الأرانب المعاملة بالإيفرمكتين إنخفاض معنوى عند مستوى (٥%) عند اليوم الأول والسابع من المعاملة فى مستوى سيرم الدم فى كل من البروتين الكلى والألبيومين مقارنة بباقى المجاميع، بينما إنخفض مستوى الجلوبيولين تدريجيا من اليوم الأول إلى اليوم السابع وحتى اليوم الـ ١٤ من المعاملة مقارنة بباقى المجاميع.
- لوحظت زيادة مستوى كل من مكونات سيرم الدم (البروتين الكلى، الألبيومين) وإنزيمات الكبد (ALT, AST) ووظائف الكلية (كرياتينين، يوريا، حامض البوليك) فى المجاميع المعاملة لتقترب من مستواها فى المجموعه الضابطة السالبة (NC) وذلك بداية من اليوم الـ ٧ والـ ١٤ من بداية المعاملة.
- إنخفض مستوى إنزيمات الكبد (ALT, AST) ووظائف الكلية (كرياتينين، يوريا، حامض البوليك) مع الوقت فى سيرم دم الأرانب المعاملة بزيت الثوم أو القرفة أو خليطهما مقارنة بالمجموعة الضابطة الموجبة (PC) أو مجموعة الإيفرمكتين (IV) خلال فترة العلاج من طفيل الجرب.
- أدى الحقن بالإيفرمكتين للأرانب المصابة بطفيل الجرب إلى زيادة معنوية عند مستوى (٥%) فى مستوى هرمون الكورتيزول، هرمونات الغدة الدرقية (T_3, T_4) عند اليوم الأول، السابع، الرابع عشر من المعاملة.
- لوحظت زيادة مستوى هرمون التستستيرون معنويا عند مستوى (٥%) فى سيرم دم الأرانب المعاملة بالإيفرمكتين أو الزيت بداية من اليوم السابع من المعاملة.
- إنخفض الـ (MAD) معنويا مستوى (٥%) بينما زاد الـ (TAC) معنويا مستوى (٥%) عند اليوم الـ ١٤ من المعاملة بالإيفرمكتين (IV) مقارنة بباقى المجاميع.

- حدث إنخفاض معنوى عند مستوى (٥%) من اليوم الأول وحتى الرابع عشر من المعاملة فى كل من حجم القذفة، تركيز الحيوانات المنوية، الحركة التقدمية، نسبة الحيوانات المنوية الحية، زمن التفاعل) بينما إرتفعت معنويا (٥%) نسبة الحيوانات المنوية المشوهة فى الأرانب المصابة بطفيل الجرب (PC) مقارنة بالمجموعة الضابطة السالبة (NC).
- وقد لوحظت زيادة فى صفات السائل المنوى المدروسة فى المجاميع المعاملة إبتداءا من اليوم الـ ٧ وحتى الـ ١٤ مقارنة بالمجموعة الضابطة الموجبة (PC).

التوصية: وجد أن كل من زيت الثوم أوزيت القرفة بتركيز ٥% مفضل فى علاج الأرانب المصابة بطفيل الجرب مقارنة بحقن الإيفرمكتين ١% مع تفادى الأثار الجانبية للإيفرمكتين ١% على إنزيمات الكبد ووظائف الكلى وصفات السائل المنوى.