

Hematological and Biochemical change due to the effect of onion (*Allium cepa*) extraction in the toxicity rabbits

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Abstract

Onion is a well-known traditional medicinal plant that has been consumed for its putative nutritional and health benefits for centuries. All research indicates that onions are used as an anti-bacterial material with a biological effect as antioxidant. This present study was carried out to investigate the possibility incidence of the growth micro pathogen on sliced onions, which was exposed to the kitchen environment for 24 hours, and then study the biochemical change on rabbits subjected to subcutaneous administration of contaminated onion juice (OE) on the rabbits. Sixteen rabbits (1000 – 1200 g) were randomly selected into 4 groups. Group A received saline water; groups, B; C; D, received 4, 8 and 12 ml of OE, respectively. The

result obtained that, the chips onion was infected by staphylococcus aureus. Subcutaneous administration of OE into rabbits revealed that, skin abscesses was observed after a week of injection for groups C and D. Serum urea and creatinine measurement were significantly ($P \leq 0.05$) increase in group C and D, the mean difference value for AST and ALT, cholesterol and triglyceride were slightly increase for groups received 8 and 12 ml of OE/Kg. As conclusion we could resume that, the toxicity effect of *S. aureus* is inhibited due to the effect of onion juice.

* Introduction

* Onion uses, benefit and chemical composition

Common onion (*Allium cepa* L.) is one of the oldest cultivated

plants, utilized worldwide as both vegetable and flavouring (Marrelli, Amodeo, Statti, & Conforti, 2019). A number of studies have proven that onion having antibacterial effect (Anyaeibunam et al., 2019; Eltaweel, 2013; S. Kim et al., 2018), antifungal properties (Kocić-Tanackov et al., 2017). Moreover, onion skin contains phenolic compounds (Akdeniz, Sumnu, & Sahin, 2018), phytochemical compound eg. organosulphur compounds and flavonoid (Miri & Roughani, 2018), which are important in terms of their health promoting effects. So that onion has many therapeutic effects such as decreasing risks of chronic diseases due to their antioxidant activity and immunomodulatory properties (Marefati et al., 2018; Soto Vargas, Gonzalez, Sance, & Galmarini, 2016).

The main antibacterial component present in onion bulbs is sulfur containing active principle allicin (Lanzotti, 2006). Allicin is unstable under physiological conditions and might quickly transform by allinase enzyme into alkyl sulfides, such as diallyl disulfide, diallyl trisulfide and diallyl sulfide (Xu et al., 2018). In intact plants, the amino acid and the enzyme are stored in separate cellular compartments (Lancaster & Collin,

1981), upon injury to plants, barriers between these compartments are broken and the alliin lyase catalyzes the beta elimination of alliin to yield pyruvate, ammonia, and allylsulfenic acid, two molecules of which spontaneously react to form allicin (Feldberg et al., 1988). Ankri and Mirelman (1999) reported that, the main antimicrobial effect of allicin is due to its chemical reaction with thiol groups of various enzymes, e.g. alcohol dehydrogenase, thioredoxin reductase, and RNA polymerase, which can affect essential metabolism of cysteine proteinase activity involved in the virulence.

S. Kim et al. (2018) concluded that, there was a positive correlation between antioxidant activities and organosulphur compounds.

*** The effect of Staphylococcus**

Staphylococcus and many serological types are the main causative agent of food poisoning due to the absorption of staphylococcus enterotoxins performed in the food (Le Loir, Baron, & Gautier, 2003). Staphylococcus aureus is an important mammals pathogen that causes a wide range of clinical infection (Tong, Davis, Eichenberger, Holland, & Fowler, 2015) as skin and soft tissue abscesses (Cheng, DeDent, Schneewind, & Missiakas, 2011),

bacteremia, pneumonia, as well as osteomyelitis and septic arthritis (Lowy, 1998). Elevated levels of superoxide anion free radicals and hydrogen peroxide generated within the tissue following infection of the mice with *S. aureus* was detected by Mal et al. (2013).

The secretion of coagulases, proteins that associate with and activate the host hemostatic factor prothrombin, and the bacterial surface display of agglutinins, proteins that bind polymerized fibrin,

S. aureus appears to be able to bind not only to damaged but also to intact endothelium. (Choi et al. 2011, Moreillon, Que and Bayer 2002). Many numbers of cell wall-associated factors have been implicated in adhesion *S. aureus* to the endothelial cell wall layer, extracellular matrix proteins, fibrin, and platelets of host, such as teichic acid of *S. aureus* (Patti, Allen, McGavin, & Höök, 1994; Weidenmaier et al., 2005). They are key virulence strategies for the pathogenesis of *S. aureus* bloodstream infections (Thomer, Schneewind, & Missiakas, 2016)

S. aureus secretes two clotting factors, coagulase and von Willebrand factor binding proteins, which together are required for attachment to and colonization of the

valvular tissue and formation of abscesses (Cheng et al., 2010; Tong et al., 2015). We tested here the hypothesis that, the onion may be the protective agent that prevents staphylococcus infection.

*** Material and method**

The present study was undertaken in Misurata university-pharmacy College. All the Biochemical procedures were carried out in Central Research Laboratory-Misurata.

*** Study Design**

1- Experimental animals: A total number of sixteen (16) adult male New Zealand white rabbits (1000-1200g), with metal wiring were housed and bred in the well-ventilated wooden cages. They were fed once daily with bread, vegetables and herbage ad libitum during all experimental period. The animals were allowed to acclimatize for two weeks, and were treated for 21 days with different doses of the onion extracts.

2- Preparation of Onion Extraction (OE): Fresh onion was obtained from the local market of Misurata city. The outer skins and ends of the onion samples were removed and washed in running tap water to remove adhering debris. Then, the onion were sliced into chips and kept out of refrigerator for 24 hours. Onions were blended

(Moulinex juice Blender) to get a clear onion juice, which it was filtered into a conical flask using a filter paper and a funnel. The extracts from contaminated onion were prepared immediately before administration into rabbits.

3- Isolation and Identification of pathogen in OE: Sample from onion juice extraction was incubated at 37°C for 18-24 hour, followed by sub-culturing on blood nutrient agar and nutrient agar media at 37°C for 24 hours.

The T-streak plate method is rapid qualitative isolation method, it is essentially a dilution technique involves spreading a loop full culture over the surface of an agar plate. The streak plate method is rapid qualitative isolation method, as described by Benson (1967).

4- Numeration of bacteria colonies on OE: Direct counting method as described by WILSON (1935) has been utilized in this study to count the numbers of bacteria in the OE by plating 1ml of OE on a petri dish with nutrient blood agar, since each colony have been originally a bacterial cell, this means numbers of colony corresponding the number of colony in the petri dish.

5- Animal treatment: The animals were randomly selected into 4 groups of 4 animals (n = 4) each, and divided

into four groups: group A was a control group received 4 ml of normal saline subcutaneously into a shaved area on the flank of each rabbit; group B,C and D received subcutaneously as the same manner 4,8 and 12 ml/Kg of OE, respectively. The experimental animals injected by contaminated onion extract weekly for three weeks.

6- Blood sample: The area of collection (jugular vein) were shaving and clean with antiseptic agent (alcohol), 5 ml The volume of blood collected was for each experimental animal, 2ml into an EDTA bottle to prevent coagulation and 3ml into plain tube to get a serum. The collection of samples was on day zero before injected animals; 7th; 14th; and 21 of experimental period.

Statistical Analysis: -

Data were subjected to tow-way ANOVA using the Post Hoc Tests to know the estimated marginal mean and profile plots of SPSS.

*** Results and discussion**

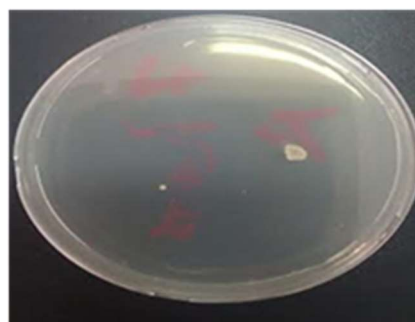


Figure (1) Direct counting method for the numeration of *S. aureus* in OE

In this study, the growing of staphylococcus has been detected on the slice of contaminated onion. The manual counting of *S. aureus* colonies recorded number of 2 colonies (n=2) of *S. aureus* for each 1m of OE. Accurate colony counting of bacteria is crucial for quantitative, precise assessment of pathogens in clinical research and diagnosis (Clarke et al., 2010). According to this work low number of bacteria in each ml of OE indicate to that, onion has a potential use against pathogenic organisms. This result agree with many finding of Anyaegbunam et al. (2019); Eltaweel (2013) who concluded that *Allium cepa* extract has antimicrobial activity against *Staphylococcus aureus*. Moreover, the finding of Akdeniz et al. (2018) and Nath et al. (2010) recorded an inhibited effect of aqueous extract or the juice of *Allium cepa* on the growth of *Escherichia coli*, *Serratia marcescens*, *Pseudomonas aeruginosa*, *Salmonella typhi*, *Streptococcus* species and *Lactobacillus odontolyticus*.



Figure (2) The effect of OE on the skin of toxicity rabbits

In this study, observable skin abscesses was recorded with groups C and D. *Staphylococcus* abscesses in animals was recorded by many research, in mice, (Kengkoom & Ampawong, 2017); rabbits (Sherertz, Carruth, Hampton, Byron, & Solomon, 1993) and human (Cheng et al., 2011). The bacterial pathogen *Staphylococcus aureus* seeds abscesses in host tissues to replicate at the center of these lesions, protected from host immune cells via a pseudocapsule (Cheng et al., 2010)

However, in group B, tissue abscess was not observed, this may partly be due to the, immunological effect of onion, which has been play a moderately role in enhancing the immune system. In various traditional medicines, onion has been classified as an immune-boosting

food (Kumar & Venkatesh, 2016; Prasanna Kumar, 2015). Patra et al. (2013) postulated that, pectic polysaccharide which was isolated from onion have an immunological activity, splenocyte, thymocyte as well as macrophage activations (Patra et al., 2013). Also many studies have claimed this property due to the presence of bioactive organosulfur compounds, prebiotic fructo-oligosaccharides and an immunomodulatory protein, lectin (*Allium cepa* agglutinin) (Clement, Pramod, & Venkatesh, 2010; Prasanna Kumar, 2015).

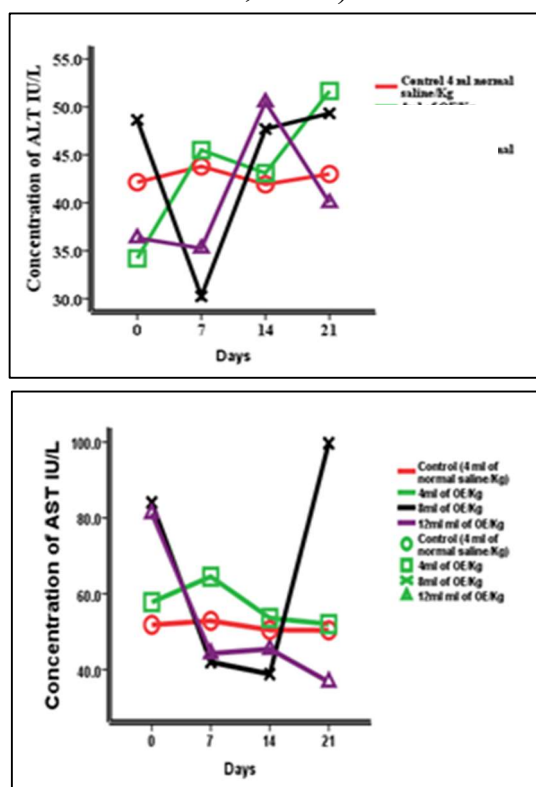


Fig. (3) The pathophysiological effect of OE on the liver function test of rabbits

As shown on the figure (3), there was no significance effect of OE on the liver function tests for all

groups. However, the results of overlap between time and treatment revealed that, for group C and D, on 7th and 14th days of treatment, AST level showed a significant ($P \leq 0.000$), decrease when compared to zero day. Moreover, the level of ALT for group received 8ml OE/Kg was significantly ($P \leq 0.27$; 0.35 and 0.33) decrease on 7th day compared to 0, 14th and 21 days, respectively.

This result shows that despite the groups were treated with repeated number of 16 pathogens for group C and 24 pathogens for group D, for time of three weeks, the improved of the liver function has been detected on the 7th day of experiment. So, this result expresses that the onion juice plays its best role as an antioxidant agent and according to the literature, the onion juice rich by high content of therapeutic agent as postulated by Gharadaghi et al. (2012); Koh and Surh (2016) who indicate onions contain both phenolic compounds and sulfur-containing compounds such as thiosulfinates and thiosulfonates. The effect of bacteriostatic concentrations of thiosulfinates (0.2 to 0.5 mM) on the growth of bacteria has been studied by Feldberg et al. (1988) they reported a pattern of inhibition characterized by a low culture density; a lower rate of growth than

in uninhibited controls and a delayed; partial inhibition of DNA synthesis and immediate and total inhibition of RNA synthesis by allicin.

In this study, the statistical analysis of the overlap between times with treatment illustrate ALT level of group received 4ml OE/Kg was significantly ($P < 0.05$) increase on 21 day compared (a) day. Moreover, the level of AS (a) group received 4ml OE/Kg was significantly ($P \leq 0.05$) on 21 day when compared to days 7th and 14th of experiment, but did not attend to the significance level when compared to day 0. This result may be attributed to the repeated infected animals by *S. aureus*. The liver is frequently involved in systemic infections, and the infected microbe can cause hepatic injury, either by direct invasion or indirectly through toxins and cytokines resulting in various types of abnormal liver function test results (Minemura, Tajiri, & Shimizu, 2014).

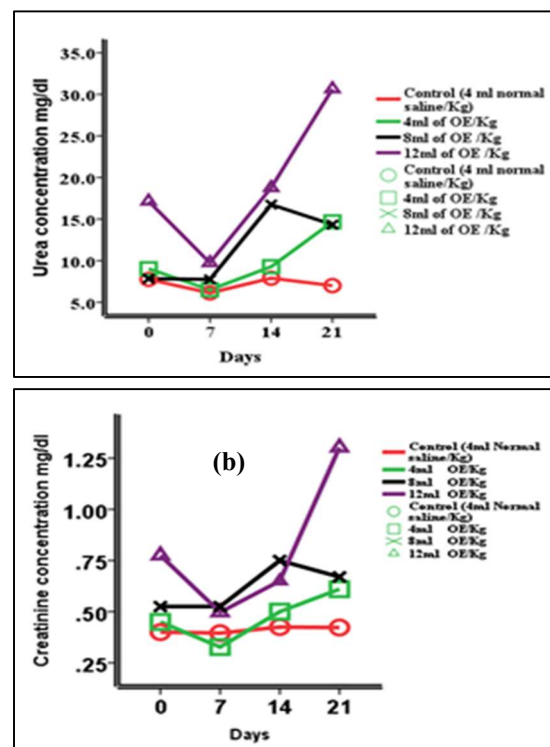


Fig. (4) The pathophysiological effect of OE on the renal function test of rabbits

In this study as shown in Figure (4, a and b), the treatment by different volume of OE affect significantly on both urea and creatinine level. The result illustrate that, urea level for group D and creatinine measurement for groups C and D have been increased significantly ($P \leq 0.05$), when compared to A and B groups. These increased of urea and creatinine levels may be as indicator of renal dis-function. Biochemically, renal failure is typically detected by an elevated serum creatinine level and proteinuria (Gharadaghi et al., 2012). In this work, the urea and creatinine levels for group received 12ml/Kg recorded the highest levels (30.6 ± 1.9

and 1.3 ± 0.31 , respectively) on day 21, this group received a relatively more number of pathogen compared to other groups and many studies refer to that, the *S. aureus* damaging the tissue according to the concentration of pathogen. Wang et al. (2004) injected rats by low-dose of staphylococcus peptidoglycan (3 mg/kg) in the jugular vein, no measurable effects was detected by them, in contrast, high-dose peptidoglycan (10 mg/kg) caused increased serum values of urea and creatinin. In contrast the study of Wills, Kerrigan, and Soothill (2005) recorded skin abscesses for all rabbits injected subcutaneously by 10^7 CFU of *S. aureus* after four days of the first injections, but no bacteria were isolated from the livers or spleens of any of the rabbits.

In this study, overlap between time and treatment by OE obtained that, urea and creatinine levels for group D on day 21 was significantly ($P \leq 0.05$) higher compared to days 0; 7th and 14th. But, for group C, urea measurement revealed a significant ($P \leq 0.01$) increase on day 14 compared to days 0 and 7th. This increased of urea may be associated with repeated infected animals by *S. aureus* and form renal abscess

In this study as shown on figure 4 (a), significant reduction in

urea measurement was detected in group D on the 7th day when compared with initial; 14th and 21 days of experimental period. In this work the reduction of urea level may be attributed partially to the protective effect of onion extract against free radicals which have been release from infected tissue. Onion contain a wide variety of phytochemicals and micro constituents such as trace elements, vitamins, fructans, flavonoids, and immunomodulatory agent lectin (ACA) which may have a protective effect against free radicals (Gharadaghi et al., 2012). Also these neutral compounds in the onion may enhance the immune system of rabbits received OE. Prasanna Kumar (2015) assessed the properties of ACA by using the macrophage cell line, they showed a significant increase in the production of nitric oxide NO, and significantly stimulated the production of pro-inflammatory cytokines (TNF- α and IL-12) (Prasanna & Venkatesh, 2015). NO is important as a toxic defense molecule against infectious organisms (Coleman, 2001). It regulates the functional activity, growth and death of many immune and inflammatory cell types including macrophages, T lymphocytes, antigen-presenting

cells, mast cells, neutrophils and natural killer cells (Coleman, 2001).

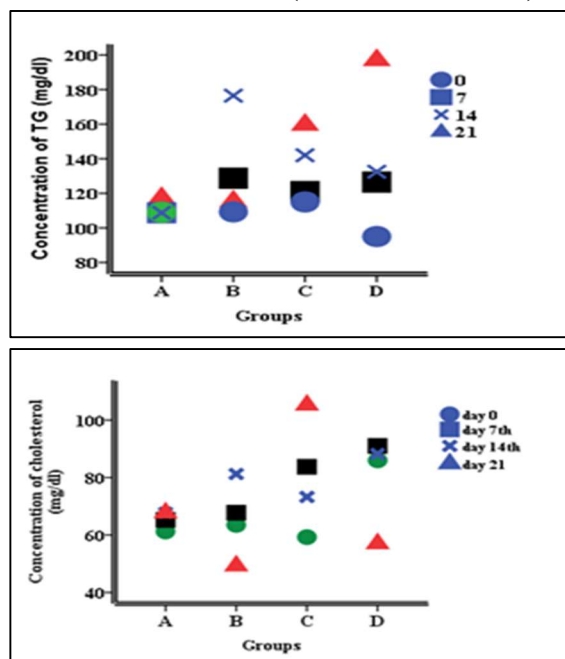


Fig. (5) The effect of OE on the cholesterol and triglyceride of rabbits.

According to the figure (5), there was no significance effect of treatment by different volume of contaminated onion on cholesterol and triglyceride levels. However, the statistical analysis for the interaction between the mean difference for time of experiment and treatment by different volume of OE revealed that, for the group D there was significant ($P \leq 0.05$) reduction in cholesterol level on day 21 compared to zero; 7th and 14th days of experiment. In contrast, for group C the cholesterol level increase significantly on day 21 compared to zero and 14th days of experimental period. There is no justification for this conflicted result, but this result may be due to the

different response of animal immune system to the treatment. Fiser, Denniston, and Beisel (1972) suggested that lipid metabolism varies with the nature of the invading microorganism as well as with the stage and duration of the infectious illness. An increased level of plasma triacylglycerols in infected rabbits by *S. aureus* during experiment was observed at a later stage (72th hour and 7th day) by Georgieva et al. (2017). Farshtchi and Lewis (1968) attributed this increased in triacylglycerols level to an inhibitory effect of Staphylococcal toxin on the activity of postheparin lipoprotein lipase which, in turn, resulted in elevation of triglycerides (Farshtchi & Lewis, 1968).

In this study the significant reduction on cholesterol level for group D on day 21 may be due to the effect of onion. According to the literature Guan et al. (2010) studied the effect of onion powder on the lipid profile of rats and they concluded that the hypocholesterolemic activity of onion powder was mediated by enhancement of fecal sterol excretion and up-regulation of liver X receptor alpha and cholesterol-7 α -hydroxylase (important regulators of cholesterol, fatty acid, and glucose homeostasis). The fecal sterol

analysis of rats fed onion powder showed that the three major phytosterols, namely β -sitosterol, campesterol and stigmasterol, were present in the feces of the two onion-fed groups but they were absent in the control group. The effects of the essential oils of onion and garlic have been investigated in cholesterol-fed rabbits by Bordia et al. (1975) cholesterol feeding increased the average lipid content of aorta, but with addition of onion or garlic oils effectively prevent lipid accumulation in the rabbit aorta.

J. Kim, Cha, Lee, and Park (2013) reported that, quercetin, a major dietary flavonoid found in onions and other vegetables, it possesses antigenotoxicity and antioxidant capacity and is capable of modulation of detoxification- and antioxidant-related gene expression in cellular and non-cellular systems. According to Gnoni, Paglialonga, and Siculella (2009), quercetin reduced triacylglycerol and very low density lipid formation by suppressing diacylglycerol acyltransferase and acetyl-CoA carboxylase activities.

Moreover, catechins, one of the bioactive compounds in onion peel extracts, may also have contributed to a favorable effect on lipid metabolism (Jaiswal & Rizvi, 2014). Inhibition of lipid absorption

by catechins is associated with the ability of catechins to form complexes with lipids and lipolytic enzymes, thus interfering with the luminal processes of emulsification, hydrolysis, micellar solubilization, and subsequent intake of lipids (Koo & Noh, 2007)

Finally, it is concluded from the results of this investigation that, the mortality rate and toxicity effect of *S. aureus* were low and that may be associated with therapeutic effect of *Allium cepa*.

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