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Biodegradation of Lycopene on AFB1 Naturally Contaminated Feed and Their Residue in Liver and Muscles Tissues of Local Male Rabbits

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Abstract

Mycotoxins are secondary fungalmetabolites that are chronic exposure ledtoresi due in biological fluids This study was carried out to find concentration of AFB1 in liver and muscle, and to study the impact of mycotoxinson effects on performance after addition of lycopene (LYC) in contaminated feed on malerabbits.

Twenty-eight local maleRabbits at age of 4-5monthswithanaveragebodyweight of 1340 gm. which are distributedbythebodyweight in fourgroups of sevenanimals. the control groupwerereceived basal dietonly(c) ,whileT^1,T^2,T^3groupsreceivedbasal diet y ralnatcontaminatedby AFB1(20.15 µg /kg Diet) exceptthe(T^1),T^2 and T^3wereLycopene 20 mg/ head and 40 mg/head respectively Cholesterol is significantly (P<0.05) decrease in e in T^2 , T^3 group compared with other groups .HDL showed higher level in T^2 , T^3 compared with T^1 and control groups, significantly (P<0.05) decrease in LDL in T^2 , T^3 groups compared with T^1 and control groups . Creatinine showed no significant change in all groups, and no change in AST, ALT enzymes.

The average concentration of AFB1 (µg/kg) was higher in muscle tissue than in liver tissue. Muscle and liver tissue control groups were not updated. The AFB1 concentration in the liver tissue (140, 2.3, 0.25) ppb appeared sequently (T1, T2, T3). In addition. While the Residues of AFB1 seen in muscle (203.1, 6.8, 0.62) ppb (T1, T2, T3), compared with AFB1 0.125 ppb.

These findings indicate that supplementation of Lycopene in rabbit feeding will decreaseresidue the liver and muscle tissues' and maintain a healthy condition for rabbits..

Keywords:AFB1, Rabbits , Residue, Lycopene , Liver,Kidney
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Introduction

Mycotoxins are toxic chemical compounds that are naturally produced by certain types of moulds (fungi)(Haque et al., 2020) .

The European Union regulated mycotoxins with Several groups such as, aflatoxins (AF), patulin , deoxynivalenol (DON), fumonisins , zearalenone (ZEA), ochratoxin A (OTAs,T-2 and ergot alkaloids. Aflatoxin was the most regulated among other mycotoxins. (Peles et al., 2019).

Due to their carcinogenic effect,AFB1 are more significant than other fungal toxins. Aflatoxin species are called according to their Green and Blue fluorescence behavior in thin layer chromatography (TLC) ,while naturally occurred in milk (B1, B2, G1, G2, M1,M2) .(De Meulenaer,2008)

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Aflatoxin (AF) B1 and their toxins can cause harmful effect in rabbits and other animal. Rabbits are the most sensitive animals to aflatoxicosis. Several effect such as reduction of eppetite , delayed growth, malabsorption of various nutrients, , decreased immunity, not useful vaccine. pathological changes in most body organs are induced by AFs ingestion. The liver and kidney also affected genetic impact carcinogenicity, teratogenicity and mutagenicity(Diekman et al., 1992) and alter on metabolism, , antioxidant status(Huang et al., 2018).and there are indirect effects on public health ,especially residue that have a negative impact on milk and milk product liver, muscle and eggs (Hussein and Atiyah.2020;Alnaemi , 2019;ALrubaye, 2016. Bintvihok, et al., 2002).

The Lycopene has been used for reduced the impact of AF (Rao and Agarwal, (1998). Lycopene is a natural material that present as a red carotenoid compound in fruits. Lycopene has antioxidant properties by Eliminating free radicals as aresult of AF toxicity . Also, Lycopene can enhance the body's antioxidant enzymes such as CAT and GSH to prevent the oxidative damage caused by AF. Lycopene enhances the body's antioxidant capacity, reduces lipid peroxidation levels, and maintains cell membrane permeabilityBasu.and Imrhan (2007)therefore Lycopene as strong antioxidant can be against aflatoxicosis(Juan et al., 2008). The role of Lycopene was clear in reducing the damage of aflatoxin by activate the stage 2 detoxification and AFB-NAC production and blocks phase 1 metabolism of AFB1 and reducing AFB-N7 that adduct in liver DNA (Tang et al., 2017 ;Reddy et al., 2006; Wang et al., 1999)

There are several techniques which have been developed to detect and measure AFs. The major immunochemical assay is the enzyme-linked immune- sorbent assay (ELISA). Other procedures are based on electrochemical and optical values such as chromatography.Linaet al.,(2012).

Materials and Methods

This experiment was conducted at the Animal House**,** College of Veterinary Medicine**,** University of Baghdad from 2020\1\27 to 2020\3\27.

Twenty-eight healthy local male rabbits were bought at age of about 4-6 months**;** with mean of body weight (1335 ± 20 gm) animals were kept in cages of animal house of Veterinary College**,** Baghdad University**.** 28 rabbits were purchased from the Drug Control Center / Ministry of Health. The animals were healthy and clinically free of internal and external parasites**,** all animals were fed on the concentrate and tap water were offered of preliminary period for (3) weeks**.**Animals were distributed into four groups that contain (7) rabbits in each group. First group fed on the concentrated diet without contamination with mycotoxinor addition Lycopene, kept as a control group(C). Thesecond group was daily fed on the same concentrate diet and given mycotoxin (T1). Third group was daily fed on the concentrate diet containedmycotoxin with lycopene 20mg/ head orally (T2) . Fourth group was daily fed on the concentrate diet containedmycotoxin with lycopene 40 mg/ head orally (T3).

Procedure of blood samples

Calculated blood serum at (4th) week and (8th) week of experimental to study the effect of mycotoxin on liver enzymes (ALT – AST) and Creatinin and total cholesterol (HDL- LDL).

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Estimation Liver Enzymes

Alanine Amino Transferase Activity-(ALT) was used in this experimental study to measure and describe the effect of mycotoxin on liver enzymes (ALT) using the ALT method (Kim et al., 2008) and the Alanine Aminotransferase DEA kit. Liver Enzyme Estimate Aspartate AST (AST) The same ALT measurement method was used and defined by Reitman and Frankel (1957). And we used the DEA kit Aspartate Aminotransferase**.**

Estimation of blood serum Creatinine

Estimation the level of creatinine in the blood according to kinetic method (Automated method) Crocker et al., 1988). And was used Creatinine kit. All four kits above were manufactured by Bio-system- Spain Company,

Estimation Total cholesterol test(Cholesterol,HDL,LDL)

Blood serum was collected at weeks 4 and 8 of experimental to study AFB1 effect on total serum cholesterol. Cholesterol is measured by Cholesterol High-Performance reagent (cat.no. 704038), Roche Diagnostics). Direct HDL-cholesterol reagent is obtained from Roche Diagnostics (Direct HDL, cat. no. 1661455) and analyzed with LDL with the same procedure (Artiss et al.1997).

Estimation AFB1 Residue in liver and muscle by HPLC

At the end of the experimental dated, 12 randomly selected Rabbits from each dietary group (4 Rabbits per cages) were slaughtered, and the livers and muscles were removed. The liver and muscles of each group were pooled separately, resulting in 4 samples of each tissue per dietary treatment. The samples were kept in disposable counter and stored at refrigerated or freezer. Aflatoxins in the tissues were extracted by:

Sample preparation

The samples (25g) have been homogenize in 100 mL 70:30 v/v methanol; water for 40 min, centrifugation centrifuged for 5 min, then 5 ml of the supernatant has been drawn, after that added with 20 mL water, and passed during the immunoaffinity column at 3 mL/min (the column plus 20 mL distilled water). The column has been has been washed with 10 mL purified water to prevent the matrix components, the column was dried by passing air to remove any residual water. then , quantitative elution has been mixed with methanol (1.4 mL) on to the column. followed by diluted water into 2 mL then moved across a 0.45 mm filter. ty, the filtrate has been inserted into the HPLC.**HPLC analyses (model SYKAMN) Germany**

Mobile phase = acetonitrile: D.W (60: 40)

Column = C18- ODS (25 cm * 4.6 mm)

Flow rate = 0.7 ml / min Detector = florescent Ex= 365 nm

, Em = 445 nm

(Lina et al., 2012)

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Statistical analysis

The statistical analysis was done using SAS 9.2 (SAS Institute Inc., Cary, NC, USA). To assess the normal distribution, the data were analyzed using Boxplot. The one-way analysis of variance (ANOVA) using the GLM procedure was used to analyze the data.
All data are given as mean ± SEM (means of 7 replicates). The differences among the means were evaluated using the Tukey HSD test at $P < 0.05$.

Results and Discussion

Creatinine, Liver enzymes and total Cholesterol(HDL,LDL)

The toxicity of Aflatoxin is related to Cancerogeneous influence in the population of humans and animals. In developed countries, sufficiently food combined regulations with levels of aflatoxin in these foods Preserve significant aflatoxin residents consumer (Abdelhamid, 2010).Table 1indicated that creatinine(e (Mg/ dl)in serum did not show any significant ($P \leq 0.05$) among the groups at 8th week and 4th week of experiment.Also, the results of ALT enzyme showed (Table 1) that there was no significant among the group that was given mycotoxin compared with control group during 8 weeks period

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Table 1. Effect dietary treatments(LYCOPENE 20-40) mg on liver enzymes (ALT and AST), creatinine, and lipid profile at 4th week and 8th week of the experiment (Mean±SEM)

	Treatments				
Period	Control	AFL	AFL+Lyco2	AFL+Luco4	*P-value*
Week 4					
ALT	23.9±4.17	21.9±1.96	19.3±4.82	18.0±1.18	0.927
AST	3.8±0.96	3.2±0.31	5.6±0.60	4.29±0.87	0.183
Creatinine	2.18±0.08	2.14±0.15	2.03±0.11	2.02±0.09	0.685
Cholesterol	**71.6±7.97 b**	**143±23.4 a**	**143±20.3 a**	**86.9±9.79 b**	**0.007**
HDL	9.57±1.22	12.7±0.89	12.9±1.164	11.9±1.50	0.225
LDL	49.1±7.05 b	120±21.69 a	122±19.2 a	66.9±8.76 b	0.004
Week 8					
ALT	10.1±4.23	14.17±0.3	18.0±2.83	12.9±2.76	0.325
AST	3.71±0.52	2.86±0.40	3.86±0.63	4.57±0.57	0.193
Creatinine	1.34±0.07	1.34±0.07	1.47±0.13	1.54±0.12	0.433
Cholesterol	130±12.5 a	132±7.19 a	87.7±6.11 b	84.5±6.5 b	0.004
HDL	10.6±0.75ab	8.7±0.68 b	10.7±1.15ab	12.3±0.71 a	0.050
LDL	121±18.54a	114.857±6.476ab	80.043±11.59bc	70.486±7.701c	0.014

a-b Means in rows with different superscript letters are significantly different (P<0.05).

This result conflicts with (Neeta Mathuria et al., 2008Abd-majeeds and Atiyah (2019) ; Hussein and Atiyah.2020) they shown significant increase in ALT in mice and male rabbits respectively .The results of AST showed no significant changes in four groups. Similar (Battacone

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et al., 2005), when dairy sheep, the consumption of pure AFB1 did not change liver enzymatic action when the daily intake extended between 32 and 128 μg/d for an exposure period of 1 wk. These enzymes: serum alanine aminotransferase (ALT) plus serum aspartate aminotransferase (AST) were existing in the cytosol of the hepatocytes.In another hand there were real significant increase in cholesterol in (T1) group compared with the other groups this result shown by (RAJMON et al .,2001). Lycopene plays a crucial role in reducing oxidative stress, particularly limiting the oxidation of low-density lipoprotein (LDL) and cholesterol. Oxidized LDL particles cause a series of events that lead to inflammatory processes, the formation of foam cells, atherosclerotic lesions, and plaque rupture, fatty streaks and plaque. The results of this study showed a real significant drop in cholesterol and LDL level in (T2, T3) groups compared with (T1) group. Also, there is a slight considerable increase of HDL that suggesting the beneficial effect of lycopene to modify the harmful impact of AFB1. This result agreed with Basu et al. (2007), Willcox. et al., (2003).

Furthermore, oxidized LDL particles damage normal endothelial function by inhibiting nitric oxide (NO) release, which is an essential relaxant of blood vessels to influences blood pressure (Willcox et al.,2003). Also, a study by Salonen et al. (1992)

indicated the protected effect of lycopene on LDL against oxidation. Thus, preventing LDL oxidation can reduce the generation of atherosclerosis and decrease the risk of cardiovascular diseases by enhancing LDL degradation and/or preventing its oxidation, inhibiting both synthesis and absorption of cholesterol, affecting both particle size and composition of LDL, rupturing of plaque and supporting endothelial functions.According to its chemical structure containing eleven conjugated double bonds, lycopene is considered an effectual antioxidant and free radical quencher. In addition to its antioxidant properties, lycopene has been recommended to reduce cholesterol levels by reducing cholesterol synthesis and increase LDL degradation (Fuhrman et al .1997; Jones et al. 1998; Rao, 2002). However, the ALP results were not significantly different among the treated groups. These results disagreed with the outcome of Ishikawa et al.'s (2017) study that regarded ALP as a significant predictor of aflatoxin intoxication. However, (Yaman et al. 2016) confirmed the toxic effects of aflatoxins to be reported by ALT and AST. ALP substantially rises in chronic and cancerous diseases of the liver and in a limited number in acute poisoning (Yaman et al., 2016). The general changeability in the appearance as well as catalytic action of hepatic enzyme group (like; cytochrome P450 and glutathionetransferase) include: biotransformation plus detoxification of AFB1 is reflected the chief cause of the detected change between kinds with the contact to the toxic effects of AF (Pier, 1992; Guerre et al., 1996). These may as well characterized the distinct residue of AFB1 found between types.

Concentration of Detection AflatoxinB1 in Liver and Muscles tissue

The residues of AFB1 were measured after 8th week of feed period in the control group and treatment groups(AFB1,AFB1+lycopene 20 mg, AFB1+lycopene 40 mg) as shown in Table 2.

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Table 2 : Residues (ppb) of AFB1 in Male Rabbits, liver, muscles received mycotoxin contaminated diet contained of AFB1 (20.15 μg / kg diet) with different dose of treatment.

Groups	Exposure Time(week)	Concentration AF In liver ppb	Concentration AF In muscles ppb
C	8th week	UDL	UDL
T^1	8th week	140	213.1
T^2	8th week	2.3	6.8
T^3	8th week	0.25	0.62

AFB1 concentration in the liver was organizing a from (0.00, 140, 2.3, 0.25) ppb according to the fourths groups respectively ,While AFB1 concentration in the muscle (breast and femoral) was organizing a from (0.00, 213.1, 6.8, 0.62) ppb respectively .

This result also agreed with Al-Rubaiy, et al., (2018) and Zohri et al., (2014) the concentration of AFB1 is increased according fish species and exposure time (European Commission (EC) ,2006). The estimation ofcarryover of AFB1 showed in special fish groups thatseen in muscle and liver tissue. On the other side , no residue presence in fish musculatures after 6 and 12 weeks of contact on another fish species , the concentration of Aflatoxin B1 is low in muscle in compared with the liver Begum et al., (2001), Bintvihok, et al., (2002) and Kenawy et al., (2009).and also in broilers (Begum, et al., 2001, Bintvihok, A, et al., 2002), Bintvihok, et al., 2006; Bintvihok., et al., 1998; Fernandez., et al., 1994b ;Arulmozhiet al., 2002).AFM1 also found inhigh concentration in the liver and low in meat and very low in egg of Alabio duck. In addition , the AFM1 is main excreatedthrough urine, feces, milk, tissues and egg after metabolized in liver. (ALrubaye, 2016;Sumantriet al., 2016).

In current study, was observed the effect of dietary Lycopene treatment on AF in T2 and T3 groups to decrease residue of AflatoxinB1 in both groups in dose dependent effects of Lycopene, higher dose led to decrease influence of Aflatoxin B1 effect,.this study agreed with Hussein and Atiyah (2020)

The difference in the concentration of AFB1 residue in the T2 and the T3 has been related to lycopene treatment, which ameloriativeaffects of Aflatoxin-induced oxidative stress. This may lead to concluded that the Lycopene being antioxidant compound that has a positive effect against Aflatoxin toxicity(Juan C et al. 2008). This important role is emphasized in Lycopene to decreased the harmful effect of Aflatoxin by activating the stage 2 detoxification and AFB-NAC production and it work to close phase 1 metabolism of AFB1, and decreased AFB-N7 that led adduct in liver DNA. This agreed with Tang et al. (2017), Reddy et al. (2006) and Wang et al. (1999).

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