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Effects of Curcumin on Hematological Parameters in Aflatoxin B1 Applied Rats

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Abstract

In this study, it is aimed to determine the possible effects of curcumin on hematological parameters in aflatoxin applied rats. Thirty eight healthy male Wistar Albino rats were used in the study. Group I animals was no applied. Animals in Group II were orally given 1 ml 10% DMSO daily for 60 days. Animals in Group III were orally given 300 mg/kg curcumin dissolved in 10% DMSO daily for 60 days. Animals in Group IV were orally given 250 µg/kg aflatoxin B1 dissolved in 10% DMSO daily for 60 days. Animals in Group V was orally given 250 µg/kg aflatoxin B1 dissolved in 10% DMSO and 300 mg/kg curcumin dissolved in 10% DMSO daily for 60 days. At the end of the study, erythrocyte count, leukocyte count, platelet count, hemoglobin amount, hematocrit value, percentage ratios of leukocyte types, mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC) were determined in blood samples taken from all animals. In the study, erythrocytes count, hemoglobin concentration, hematocrit value and MCHC level in the aflatoxin applied rats significantly decreased compared to the control group ($p<0.05$). MCV level in the aflatoxin applied rats was found significantly higher compared to the control group ($p<0.05$). In the group in which aflatoxin and curcumin were administered together, erythrocytes count, hemoglobin concentration, hematocrit value and MCHC levels were found to be significantly higher compared to the group administered only aflatoxin ($p<0.05$). In the study, the leukocyte count significantly decreased in the aflatoxin group compared to the control group ($p<0.05$). Granulocyte and monocyte percentage significantly increased depend on aflatoxin application ($p<0.05$). In the group in which aflatoxin and curcumin were administered together, the leukocyte count significantly increased compared to the aflatoxin group ($p<0.05$). We concluded that curcumin may alleviate the abnormalities in hematological parameters resulting from aflatoxicosis.

Key words: Aflatoxin, Curcumin, Hematological Parameters, Rats

INTRODUCTION

In parallel with the economic developments of the countries, the demands of the societies for meat, milk and other animal products are increasing in order to get the necessary protein and essential minerals with nutrients (12). There are different environments and contaminations in which foodstuffs are exposed in many stages from the field and industrial production to consumption. Depending on any of these stages, the presence of mycotoxins in foodstuffs remains one of the most important obstacles to the developing food sector (19). Although there are many mycotoxins in the world, aflatoxins are the most common seen mycotoxins. Aflatoxin B1 is a secondary metabolite with hepatotoxic properties produced by Aspergillus species such as Aspergillus flavus, Aspergillus nomius and Aspergillus parasiticus. These cause contamination during the production and processing of foods and feeds (32). Recent studies have shown that humans and livestock are sensitive to aflatoxins and that aflatoxins have acute toxicity, mutagenicity and carcinogenic effects (16). Mycotoxins cause hepatotoxicity, nephrotoxicity, hepatocarcinogenicity in humans and animals due to their various negative effects (15). It is reported that the damage of tissues and cells due to aflatoxin intoxication especially causes the decrease in protein synthesis in the liver and intestines (7, 26). As a

result of aflatoxin B1 damaging hematopoietic organs, it is reported that it causes negative changes especially in erythrocyte counts and hemograms (33), as well as it reduced the levels of parameters such as hemoglobin and hematocrit value (7, 26). It is suggested that the decrease in erythrocyte counts indicates inhibition of protein synthesis (24, 26, 42). It is reported that stress caused by aflatoxin on liver and kidney tissue decreases the total erythrocyte count, which is the result of decreased erythropoietin activity depending on aflatoxin B1 (30, 36).

Curcumin(1,7-bis(4-hydroxy-3methoxyphenyl)-1,6-hepadien-3,5-dion) is a herbal phenolic compound that is abundant in the roots of the Curcuma Longa plant. It is used as a coloring and spice in foods. It is among the notifications that curcumin can prevent oxidative stress occurring in erythrocyte membranes and can reverse the negative effects of oxidative stress on plasma proteins (22, 43). Curcumin has been reported to have positive effects on mycotoxins-induced cell damage, free radical release and lipid peroxidation (11, 25).

Based on the above information, this study is planned to determine the possible effects of curcumin on hematological parameters in rats administered aflatoxin.

MATERIALS AND METHODS

Thirty eight healthy male Wistar Albino rats (2 weeks old) were used in the study. In the study, suitable living conditions (heat, humidity and light) were provided for the rats. The animals were divided into five groups and fed for 60 days with standard rat food as ad libitum. This study protocol was approved by Selçuk University Experimental Medicine Research and Application Center Ethics Committee (Report no. 2018-26).

Group I (K) (n=6): Nothing was applied.

Group II (DMSO) (n=6): The animals were orally given 1 ml 10% DMSO daily for 60 days.

Group III (Cur) (n=6): The animals were orally given 300 mg/kg curcumin (Sigma Aldrich, St. Louis, MO, USA) dissolved in 10% DMSO daily for 60 days.

Group IV (AFB1) (n=10): The animals were orally given 250 μg/kg aflatoxin (Acros Organics, Geel, Belgium) B1 dissolved in 10% DMSO daily for 60 days.

Group V (AFB1+Cur) (n=10): The animals was orally given 250 μg/kg aflatoxin B1 dissolved in 10% DMSO and 300 mg/kg curcumin dissolved in 10% DMSO daily for 60 days (21, 31).

In the study, blood was taken from animals in all groups at the end of 60 days. In these blood samples, erythrocyte count, leukocyte count, platelet count, hemoglobin amount, hematocrit value, percentage ratios of leukocyte types, mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC) were determined. Erythrocyte count, leukocyte count, platelet count, hemoglobin amount, hematocrit value, percentage ratios of leukocyte types, MCV, MCH and MCHC levels were measured by the impedance method in the Abbott Cell Dyn 1800 autoanalyser.

The data obtained from the study were analyzed by one-way ANOVA (SPSS 19). Differences among the groups were determined by Duncan's multiple range test. Differences were considered significant at $p<0.05$.

RESULTS

In the study, the effects of curcumin application in rats treated with aflatoxins on erythrocyte count, hemoglobin, hematocrit, MCV, MCH and MCHC levels are given in Table 1 and its effects on leukocyte count, granulocyte, lymphocyte, monocyte and platelet levels are given in Table 2.

Table 1. The effects of curcumin on erythrocyte count, hemoglobin, hematocrit, MCV, MCH and MCHC levels in aflatoxin-applied rats (Mean±SE).

	Erythrocyte count ($x\ 10^6/mm^3$)	Hemoglobin (g/dl)	Hematocrit (%)	MCV (μm^3)	MCH (pg)	MCHC (%)
Group I	7.25±0.14^{a}	13.23±0.42^{ab}	38.12±0.60^{a}	52.58±0.84^{b}	18.27±0.53	34.72±0.55^{a}
Group II	7.21±0.44^{a}	13.18±0.29^{ab}	38.37±0.77^{a}	53.22±2.22^{ab}	18.28±0.66	34.35±1.04^{a}
Group III	7.39±0.47^{a}	13.55±0.38^{a}	38.93±0.69^{a}	52.68±2.55^{b}	18.33±1.01	34.82±0.79^{a}
Group IV	5.32±0.40^{b}	9.43±0.60^{c}	31.28±0.43^{c}	58.80±1.54^{a}	17.73±0.60	30.15±0.71^{b}
Group V	6.57±0.33^{a}	11.79±0.41^{b}	35.56±0.89^{b}	54.12±1.87^{ab}	17.95±0.56	33.16±0.85^{a}

$^{a-c}$ The difference between mean values with different superscripts in the same column is significant at the $p<0.05$ level.

Table 2. The effects of curcumin on leukocyte count, granulocyte, lymphocyte, monocyte and platelet levels in aflatoxin-applied rats (Mean±SE).

	Leukocyte count ($x\ 10^3/mm^3$)	Granulocyte (%)	Lymphocyte (%)	Monocyte (%)	Platelet (K/µl)
Group I	10.44±0.66^{a}	16.62±0.76^{bc}	79.52±2.54	2.87±0.23^{b}	628.33±42.34
Group II	10.63±0.90^{a}	16.55±0.66^{bc}	79.30±1.56	4.15±0.34^{a}	638.67±29.57
Group III	10.38±0.63^{a}	15.23±0.45^{c}	81.15±1.73	3.62±0.41^{ab}	634.17±41.70
Group IV	6.07±0.69^{c}	18.97±0.67^{a}	76.62±0.74	4.41±0.30^{a}	581.50±36.39
Group V	8.24±0.58^{b}	18.43±0.55^{ab}	77.63±1.44	3.94±0.25^{a}	597.80±35.51

$^{a-c}$ The difference between mean values with different superscripts in the same column is significant at the $p<0.05$ level.

DISCUSSION

In the study, erythrocyte count, hemoglobin concentration and hematocrit value from hematologic parameters of the rats administered aflatoxin for 60 days showed a significant decrease compared to the control group ($p<0.05$, Table 1). While MCV level, which is one of the erythrocyte indices, was found to be significantly higher with aflatoxin application compared to the control group ($p<0.05$, Table 1), the MCHC level was significantly lower than control group ($p<0.05$, Table 1). In the study, it was determined that erythrocyte count, hemoglobin concentration and hematocrit value in the group which aflatoxin and curcumin were administered together with the same duration were significantly higher compared to the group that only aflatoxin was applied ($p<0.05$, Table 1). With the application of curcumin together with aflatoxin, the change in the level of MCHC from erythrocyte indices was significant compared with aflatoxin group ($p<0.05$, Table 1). A marked decrease in the MCV level with the application of curcumin together with aflatoxin was observed, but this decreament was not impotant. There was no significant difference among the groups in terms of MCH level.

The hematopoietic system acts as a mirror that reflects changes occurring the body depending on exposure to chemicals, toxic agents and drugs in humans and animals (2, 44). Aflatoxins have harmful effects in terms of many tissues and organs, especially liver, kidneys and hematopoietic system, in humans and animals (30, 36). In the study, negative changes in erythrocyte count, hemoglobin and hematocrit value related to aflatoxicosis can be attributed to many factors. These include the fact that aflatoxin B1 directly affects erythropoiesis in the bone marrow and decreases the production of erythrocytes, as well as the rapid destruction in erythrocytes produced by spleen and released from there into the circulation (30, 36). The significant decrease in hemoglobin level depending on aflatoxicosis observed in the study appears to reflect macrocytic hypochromic anemia. The reason for the decrease in hemoglobin level can be attributed to decrease in erythrocyte count and impairing of heme biosynthesis in the bone marrow (30, 36). On the other hand, it is suggested that aflatoxin B1 may cause hemolytic anemia depending on hemopoietic cellular defects, which may contribute to negative changes in erythrocyte count and hemoglonin level (2, 5, 40). It is suggested that another factor which causes negative changes in hematological parameters may be down-regulation of erythropoietin activity depending on the stress caused by aflatoxin in kidneys (30, 36). It is also reported that aflatoxins reduce serum total iron binding capacity and cause protein synthesis inhibition and low serum albumin level (1, 20, 23).

There are several reasons for the decrease in hemoglobin level depending on aflatoxicosis, such as aflatoxin B1 increases the autooxidation rate of oxyhemoglobin and shortens cell life time with negatively affecting ATP energy support and sugar transfer as a result of aflatoxin B1 binding to cell membrane proteins (6, 8, 14). The decrease in erythrocyte count and hematocrit value is attributed to hemolysis caused by lipid peroxidation of plasma membrane due to aflatoxin B1 (29).

Curcumin, a yellow substance obtained from the roots of the Curcuma longa plant, is a crystalline compound. Since it has many biological activities, it is claimed that curcumin is used as a hepatoprotective based on its antioxidant and anti-inflammatory properties, and it is also useful in various types of cancer (3, 17, 39). In the study, positive changes in erythrocyte count, hemoglobin amount and hematocrit value as a result of curcumin application together with aflatoxin support the reports that curcumin minimizes the negative changes occurring hemogram. It is stated that curcumin increases erythropoiesis, supports cell membrane stabilization and prevents cellular damage caused by reactive oxygen species, thereby restoring the amount of blood (2, 10, 35). It is reported that curcuminoids extracted from turmeric are a natural absorbent, can absorb toxins through polar ends, besides detoxifying epoxides, inducing drug metabolizing enzymes such as glutathione-S-transferase and they increase their detoxifying properties against toxins (18, 29, 37, 38). It is stated that these properties reflect positive effects of curcumin on changes in blood parameters related to aflatoxin (29). In this study, positive findings related to curcumin can be attributed to the above mentioned features of curcumin.

In the study, the leukocyte count, which is one of the hematological parameters, significantly decreased in aflatoxin B1 applicated rats compared to the control group ($p<0.05$, Table 2). When leukocyte fractions were examined, it was determined that while the percentage of granulocytes significantly increased depending on aflatoxin application ($p<0.05$, Table 2), the percentage of monocyte from mononuclear leukocytes significantly increased ($p<0.05$, Table 2) and the change in the percentage of lymphocyte was not significant. In terms of the number of platelets determined in the study, there was no significant difference between the groups depending on aflatoxin application. In the study, while the leukocyte count of group with curcumin application together with aflatoxin was significantly increased compared to the aflatoxin group ($p<0.05$, Table 2), it was still significantly lower than the control group ($p<0.05$, Table 2). In the study, the changes determined in the percentages of granulocytes and monocyte of group with curcumin application together with aflatoxin were not statistically significant compared to the aflatoxin group.

In the study, the significant decrease in the leukocyte count in the aflatoxin group compared to the control group ($p<0.05$, Table 2) is evaluated as a reflection of the immunosuppressive effect caused by aflatoxin B1 (27, 28, 34, 36). The decrease in total leukocyte count depending on aflatoxin is in agreement with the findings of various researchers (2, 8). In the study, the reason of high granulocyte percentage determined in aflatoxin group may be the result of lymphopenia, as well as may be an indicator of the persistence of aflatoxin B1 related inflammation (13). The significant increase in the amount of monocytes can also be considered as a reflection of the inflammatory condition caused by aflatoxin in various organs and tissues. The decrease in the total leukocyte count may be the result of various factors such as impaired immunogenesis, decreased phagocytic activity, thymus aplasia, suppression of cell-mediated immunity and suppression in leukocyte migration, besides general suppression caused by aflatoxin B1 in the hemopoietic system (4, 28, 36). The fact that curcumin application has reducing effect negative results caused by aflatoxin B1 on the hematopoietic system supports that herbal products contains antioxidative and anti-inflammatory agents. Enhancing effect on total leukocyte count of Curcuma Longa extract and curcumin shows that curcumin has immunostimulatory activity (9, 36). On the other hand, it is suggested that curcumin as an anti-inflammatory agent can disrupt the interaction between circulating cells and endothelium, thereby improving the survival time of leukocytes (3, 41).

CONCLUSION

The results we obtained in the study are considered important in terms of revealing that the administration of curcumin together with aflatoxin for 60 days alleviated the negative changes in hematological parameters related to aflatoxicosis.

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REFERENCES

1. Abbès S, Ben Salah-Abbès J, Abdel-Wahhab MA, Ouslati R. Immunotoxicological and biochemical effects of Aflatoxins in rats prevented by Tunisian Montmorillonite with reference to HSCAS. Immunopharmacol Immunotoxicol, 2010; 32(3): 514-522.
2. Abd Allah OA, Fararh KM, Farid AS, Gad FA. Hematological and hemostatic changes in aflatoxin, curcumin plus aflatoxin and curcumin treated rat. Benha Vet Med J, 2017; 32(2): 151-156.
3. Abdelrachied HG. Haematological parameters in rats treated with royal jelly and curcumin antioxidants after CCL4haemotoxicity. J Adv Biol, 2015; 7(1): 1214-1219.
4. Abdel-Rahman TM, Ali DMI, Abo-hagger AA, Ahmed MS. Efficacy of banana peel in reduction of aflatoxin toxicity in rats. J Agric Chem Biotechn, Mansoura Univ, 2017; 8(10): 251-259.
5. Abdel-Wahhab MA, Nada SA, Khalil FA. Physiological and toxicological responses in rats fed aflatoxin-contaminated diet with or without sorbent materials. Anim Feed Sci Technol, 2002; 97(3-4): 209-219.
6. Abdel-Wahhab KG, Mannaa FA, Abdel-Wahhab MA. Panax ginseng C.A. Meyer extract protects rat erythrocyte from the oxidative damage induced by the synergistic effects of subchronic treatment with aflatoxin B1 and fumonisin. British J Med Medic Res, 2014; 4(9): 1883-1901.
7. Abeena B, George AJ, Mohammed Shejir R, Nair ND, Manomohan CB. Haematobiochemical changes of layer chicken in experimental Aflatoxicosis. Indian Vet J, 2015; 92(10): 84-86.
8. Al-Saad LA, Al-Badran AI, Al-Jumayli SA. *Extra cellular ability* of bacillus subtilis and psedomonas fluoresence to degrade aflatoxin B1 produced by aspergillus flavus. World J Pharmaceut Res, 2015; 4(8): 157-173.
9. Antony S, Kuttan R, Kuttan G. Imunomodulatory activity of curcumin. Immunol Invest, 1999; 28(5-6): 291-303.
10. Banji D, Pinnapureddy J, Banji OJ, Kumar AR, Reddy KN. Evaluation of the concomitant use of methotrexate and curcumin on Freund's complete adjuvant-induced arthritis and hematological indices in rats. Ind J Pharmacol, 2011; 43(5): 546-550.
11. Biehl ML, Buck WB. Chemical contaminants: Their metabolism and their residues. J Food Protect, 1987; 50(12): 1058-1073.
12. Brameld JM, Parr T. Improving efficiency in meat production. Proc Nutr Soc, 2016; 75(3): 242-246.
13. Chang CF, Hamilton PB. Refractory phagocytosis by chicken thrombocytes during aflatoxicosis. Poult Sci, 1979; 58(3), 559-561.
14. Cloherty EK, Livine KB, Carruthers A. The red blood cell glucose transporter presents multiple nucleotide sensitive sugar exit sites. Biochemistry, 2001; 40(51): 15549-15561.
15. Dall'Asta C, Mangia M, Berthiller F, Molinelli A, Sulyok M, Schuhmacher R, Krska R, Galaverna G, Dossena A, Marchelli R. Difficulties in fumonisin determination: the issue of hidden fumonisins. Anal Bional Chem, 2009; 395(5): 1335-1345.
16. Di Gregorio MC, Bordin K, Souto PCMC, Corassin CH, Oliveira CAF. Comparative biotransformation of aflatoxin B1 in swine, domestic fowls, and humans. Toxin Rev, 2015; 34(3): 142-150.
17. Gandhi P, Khan Z, Chakraverty N. Soluble curcumin: A promising oral supplement for health management. J Appl Pharmaceutical Sci, 2011; 1(2): 1-7.
18. Gowda NK, Ledoux DR, Rottinghaus GE, Bermudez AJ, Chen YC. Efficacy of turmeric (Curcuma longa), containing a known level of curcumin, and a hydrated sodium calcium aluminosilicate to ameliorate the adverse effects of aflatoxin in broiler chicks. Poult Sci, 2008; 87(6): 1125-1130.
19. Guerre P. Worldwide mycotoxins exposure in pig and poultry feed formulations. Toxins, 2016; 8(12): 350.
20. Harvey RB, Kubena LF, Phillips TD, Corrier DE, Elissalde MH, Huff WE. Diminution of aflatoxin toxicity to growing lambs by dietary supplementation with hydrated sodium calcium aluminosilicate. Am J Vet Res, 1991; 52(1): 152-156.
21. Irene II, Onyechi O. Effect of dietary incorporation of vernonia amygdalina. Del on AFB1 induced hepatotoxicity in weanling albino rats. Jamaican J Sci Technol, 2004; 15: 32-36.
22. Kalpravidh RW, Siritanaratkul N, Insain P, Charoensakdi R, Panichkul N, Hatairaktham S, Srichairatanakool S, Phisalaphong C, Rachmilewitz E, Fucharoen S. Improvement in oxidative stress and antioxidant parameters in beta-thalassemia/Hb E patients treated with curcuminoids. Clin Biochem, 2010; 43(4-5): 424-429.
23. Kaneko JJ. Clinical Chemistry of Domestic Animals (4th ed.). San Diego, CA: Academic Press, 1989.
24. Kubena LF, Harvey RB, Huff WE, Elissalde MH, Yersin AG, Phillips TD, Rottinghaus GE. Efficacy of a hydrated sodium calcium aluminosilicate to reduce the toxicity of aflatoxin and diacetoxyscirpenol. Poult Sci, 1993; 72(1): 51-59.
25. Murphy PA, Hendrich S, Landgren C, Bryant CM. Food mycotoxins: An update. J Food Sci, 2006; 71(5): 51-65.
26. Naseem MN, Saleemi MK, Abbas RZ, Khan A, Khatoon A, Gul ST, Imran M, Sindhu ZUD, Sultan A. Hematological and serum biochemical effects of aflatoxin B1 intoxication in broilers experimentally infected with fowl adenovirus-4 (FAdV-4). Pak Vet J, 2018; 38(2): 209-213.
27. Pestka JJ, Bondy GS. Alteration of immune function following dietary mycotoxin exposure. Can J Physiol Pharmacol, 1990; 68(7): 1009-1016.
28. Pier AC, McLoughlin ME. Mycotoxin suppression of immunity. In: J. Lacey (Ed.) Trichothecenes and Other Mycotoxins, 1985; 507-519.
29. Prajapati A, Verma Y, Swamy M, Dubey A. Efficacy of herbal binder in aflatoxin b1 induced toxicity on haematological profile in wistar rats. Indian J Field Vet, 2013; 9(2): 16-19.
30. Reddy RV, Taylor MJ, Sharma RP. Studies of immune function of CD-1 mice exposed to aflatoxin B1. Toxicology, 1987; 43(2): 123-132.
31. Reeta KH, Mehla J, Pahuja M, Gupta YK. Pharmacokinetic and pharmacodynamic interactions of valproate, phenytoin, phenobarbitone and carbamazepine with curcumin in experimental models of epilepsy in rats. Pharmacol Biochem Behav, 2011; 99: 399-407.
32. Rustemeyer SM, Lamberson WR, Ledoux DR, Rottinghaus GE, Shaw DP, Cockrum RR, Kessler KL, Austin KJ, Cammack KM. Effects of dietary aflatoxin on the health and performance of growing barrows. J Anim Sci, 2010; 88(11): 3624-3630.
33. Sakhare PS, Harne SD, Kalorey DR. Effect of toxiroak polyherbal feed supplement during induced aflatoxicosis, ochratoxicosis and combined mycotoxicoses in broilers. Vet Arhiv, 2007; 77(2): 129-146.

34. Sharma RP. Immunotoxicity of mycotoxins. J Dairy Sci, 1993; 76(3): 892-897.
35. Sharma V, Sharma C, Paliwal R, Pracheta SS, Sharma S. Ameliorative effects of Curcuma longa and curcumin on aflatoxin B1 Induced serological and biochemical changes in kidney of male mice. Asian J Biochem Pharmaceut Res, 2011a; 2: 338-351.
36. Sharma V, Sharma C, Sharma S. Influence of curcuma longa and curcumin on blood profile in mice subjected to aflatoxin B1. IJPSR, 2011b; 2(7): 1740-1745.
37. Soni KB, Lahiri M, Chackradeo P, Bhide SV, Kuttan R. Protective effect of food additives on aflatoxin-induced mutagenicity and hepatocarcinogenicity. Cancer Lett, 1997; 115(2): 129-133.
38. Srinivas L, Shalini VK, Shylaja M. Turmerin: A water soluble antioxidant peptide from turmeric (Curcuma longa). Arch Biochem Biophys, 1992; 292(2): 617-623.
39. Swamy AV, Gulliaya S, Thippeswamy A, Koti BC, Manjula DV. Cardioprotective effect of curcumin against doxorubicin-induced myocardial toxicity in albino rats. Indian J Pharmacol, 2012; 44(1): 73-77.
40. Tung HT, Cook FW, Wyatt RD, Hamilton PB. The anemia caused by aflatoxin. Poult Sci, 1975; 54(6): 1962-1969.
41. Vachharajani V, Wang SW, Mishra N, El Gazzar M, Yoza B, McCall C. Curcumin modulates leucocytes and platelets adhesion in murine sepsis. Microcirculation, 2010; 17(6): 407-416.
42. Valchev I, Kanakov D, Hristov TS. Investigations on haematological parameters and bone marrow morphology in broiler chickens with experimental aflatoxicosis. Agri Sci Technol, 2014; 6: 417-22.
43. Weeraphan C, Srisomsap C, Chokchaichamnankit D, Subhasitanont P, Hatairaktham S, Charoensakdi R, Panichkul N, Siritanaratkul N, Fucharoen S, Svasti J, Kalpravidh RW. Role of curcuminoids in ameliorating oxidative modification in β-thalassemia/Hb E plasma proteome. J Nutr Biochem, 2013; 24(3): 578-585.
44. Yuan G, Dai S, Yin Z, Lu H, Jia R, Xu J, Song X, Li L, Shu Y, Zhao X. Toxicological assessment of combined lead and cadmium: acute and sub-chronic toxicity study in rats. Food Chem Toxicol, 2014; 65: 260-268.