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Effect of prebiotic and/ or antibacterial drug on performance of broiler infected with E.coli

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Abstract : This study was conducted in order to investigate the beneficial effect induced by lysozyme , betain tylosine and/or colistine on performance of broiler chickens in presence of infection with avian pathogenic *E.coli* (APEC) treated with tylosine and or colistine.360 one old day broiler chick divided into 9 equal groups; 40 chicks in each. Groups 2-8 experimentally infected with *E.coli* groups 2, 3, 4 and 6 treated with tylosine, gr 2 and 8 treated with colistine sulphate , groups 4 and 5 received lysozymes while groups 6 and 7 were given Betain. Birds of groups 1 and 9 were kept as negative and positive control; respectively. Average body weight (ABW), organ body weight (liver, intestine, Gizzard and Bursa) as well as organ body weight ratio (BWR) at 3rd, 7th and 10th dpi were calculated together with feed conversion rate (FCR) and average feed intake. Samples from liver and intestine were collected for histopathological examination. The best FCR was in group (6) that received tylosine and betain (1.44) followed by (1.46) group (7) which received betain then followed 1.49 of gr (5) received lysozyme then followed by group (2) which received tylosine and colistine and group (4) which received tylosine and lysozme those showed similar result 1.50 followed by group (3) received tylosine which was 1.51 then control negative group (1) which was 1.53 then the lowest 1.72 in *E.coli* infected nontreated. Organ BWR in the 10th days post challenge the highest is spleen of group 7 received betaine which was 0.15, followed similar results (0.13) of group 6 and group 5 , followed by group 4 which was 0.12 , then groups 8, control positive group group 9 and gr2 has similar results which was 0.11, finally group 1 which is 0.07. Concerning liver BWR by 10th days post challenge the highest was group 7 which was 4.09, followed by gr 6 which was 3.87, followed by group 5 which was 3.81, followed by group 4 which was 3.79, followed by group 2 which was 3.75, followed by control negative group 1 which was 3.50, followed by control positive group 9 which was 3.45, followed by group 3 which was 2.99, followed by group 8 which was 2.09. concerning intestine body weight ratio by 10th days post infection the highest was group 4 which was 7.19, followed by group 2 which was 6.66, followed by group 5 which was 6.24, then group 7 (betaine) which was 6.20, followed by group 6 which was 6.12, then group 3 received tylosine which was 6.10, followed by group 8 which was 5.96, followed by control positive group 9 which was 5.83, and finally group 1) which was 5.60.
Gizzared –proventriculus BWR it was found by 10th days post infection that highest ratio was gr 4 which was 4.47 followed by group 2 which was 4.16 followed by gr 3 which was 4.07 followed by gr 5 which was 4.04, followed by group 8 which was 3.66, followed by groups 6 and group 7 which showing same results 3.65, then followed by group 1 which was 3.60 and finally group 9 which was 3.57. Bursal BWR by the 10th days post infection the highest was

group 7 which was 0.21, followed by g 6 which was 0.20, followed by group 4 and group 8 which show similar results 0.18, followed by group 3 and group 5 which also show similar results 0.17, then groups 2 and group 9 are showing similar results which was 0.16, finally group 1 which was 0.15.
Histopatholgical finding of liver are varied from group to another as group one shows no changes while gr 2,6,7 and 8 showed mild changes after challenge in form of mild congestion of portal vein on the other hand control positive gr 9 showed severe congestion of the portal vein and sinusoids the hepatocytes suffering from vacuolar degeneration in the cytoplasm with disorganization of the hepatic cord, groups 3,4 and 5almost showed the same lesion in the form of mild congestion of the portal vein, congestion of the central vein and vacuolar degeneration of hepatocyte which considered a reversible condition. Concerning histopathological finding of intestine, group (1) control negative group showing no lesions and normal histopathological section as shown in fig.(6), while gr (9) control positive showing severe congestion of the blood vessels in the sub mucosa accompanied with mild edema with inflammatory cells inflation in both the mucosa and the sub mucosa, while chickens groups 2,4,5 and 8 showing mild inflammatory cell infiltration as shown in fig (8), while groups 3,6 and 7 showing inflammation with inflammatory cell infiltration in mucosa and submucosal layer as shown in fig (9).this results revealed that antibiotic colistine and lysozymes control *E.coli* and prevent destructive effect on intestinal mucosa.
It could be concluded that antibiotics used against avian pathogenic *E.coli* still of value in control of infection by improving performance either single or in combination. The used prebiotic showed to play an important role in improving productivity of infected chickens. The used combinations are safe and effective. Therefore, we can advice to use of combination between antibacterial and prebiotic for prevention and control of infection in high risk facing poultry industry.
Key words : broiler performance, prebiotic, *E.coli*, tylosine, lysozyme , betaine, colistine.

Introduction

Colibacillosis considered one of the most important poultry disease caused by avian pathogenic *E.coli* (APEC) which is responsible for several extra intestinal pathological conditions in broiler chickens such as airsacculitis, colisepticemia and cellulitis, the most prevalent virulent strain that isolated from many outbreaks in broiler was serogroup O78[1] causing severe economic losses in the form of increase mortality rate, carcass condemnation and cost of treatment[2] by using sensitive antibacterial medication[3]. Antibacterial medications have been used in poultry industry for several years[4] used as growth promoters, disease prophylaxis and therapeutic treatment for many infectious diseases that affects poultry industry together with enhancing immune function[5,6,7,8]. One of mostly used antibacterial antibiotic is Colistine sulphate which used in poultry industry controlling enteric pathogens resulting in improves live weight gain increases and the feed conversion rate [9] and efficient control of APEC[10]. also tylosine sulphate is widely used in poultry industry in control of necrotic enteritis (NC) and indirectly improve poultry performance [11], as growth promoters in subtherapeutic level [12] and treatment of Mycoplasma gallisepticum (MG)[13] unfortunately many adverse conditions rise up due to hazard antibiotic use including antibiotic resistant- pathogens together with antibiotic residues in poultry which directly affecting human health[14,15], this create persistent needs of production safe broilers meat with best quality carcuss by using of non antibiotics feed additives helps in better carcass yield together with better protection from poultry pathogens, this products such as lysozymes and Betain. Betain not only has an great role as effective osmoregulator to overcome heat stress in broiler chickens[16,17] but also Betaine could improve the production performance and the quality of the carcass, as well as to reduce the wet of the chicken house and help to overcome coccidiosis and anti-stress effect[18] which indirectly improve weight gain and feed conversion rate, moreover betain also improves relative bursal weight[19], recently many researcher suggested that at an appropriate dose of betaine may spare some quantity of dl-methionine and dietary energy to support the growth process of heat-stressed broilers resulting in improve live weight and feed intake [20].

Not only betain is used in modern poultry industry but also lysozyme, the persistence need of lysozyme as safe and effective potential alternative for antibiotics due to increased antibiotic resistance together with the fact of huzzard effect of antibiotic residues in processed poultry carcass on human being[21], Lysozyme could be

a potential candidate to eliminate *Clostridium perfringens* and improves growth performance in broiler chickens [22,23]

From the above mentioned data this research designed in order to compare the effect of usage of prebiotic (lysozyme and betain) and antimicrobial drugs (Colistin sulphate and tylosine) each alone or in combination on performance of broiler chickens infected experimentally with *E.coli*.

Material and methods

1- Experimental Chicks:

One day old 360 commercial cobb broiler chicks were used in the study. The used birds were divided into 9 equal groups 40 chicks in each were reared under field condition. Groups 2-8 experimentally infected with *E.coli*, groups 2,3,4 and 6 treated with tylosine antibiotic (Tylox ®) ,group 2 and 8 treated with colistine sulphate , groups 4 and 5 received lysozymes while groups 6 and 7 received Betain while groups 1 and 9 kept as negative and positive control respectively, positive control were infected orally with 0.5ml of E coli O78 K80 H11 strains containing 1 x 10^4 viable microorganism /ml phosphate buffered saline (PBS).

2-Bacterial strain :

E.coli strain (O78 K80 H11) used were orally inoculated with infected groups in rate of 1 ml of saline containing 10^8 colony forming unit (CFU) E. coli/ ml [24]

3- prebiotic:

*** Lysozyme10%:** produced by Nanchang lifeng Industry and Trading Co.,Ltd., Batch no. 20131030 , exp. date : October 2016 .

Dosage 0.5 gm/L drinking water.

*** Betaine Anhydrous 98% :** produced by Nanchang lifeng Industry and Trading Co., Ltd., Batch no. 20131106, exp. Date : june 2016.

Dosage 1 gm/L drinking water.

4- Antibiotics:

*** Colistin sulphate 6 MIU:** each gm contains 6000.000 IU colistine sulphate. Lot No. 150415 . Jordan Vet. and Agr. Med. Ind. Co – Amman – Jordan.

*** Tylox® :** tylosine water soluble powder 100gm - Lot. No. 150118. Jordan Vet. and Agr. Med. Ind. Co – Amman – Jordan.

5- Feed conversion rate (FCR):

It was calculated by total weight/g of food consumption / birds of specific group during a given period over total weight gain /g of the same group birds during a given period [including weight gain of birds which died during the given period] according to [25].

6- organ body weight ratio :

It was calculated by dividing organ weight on average body weight in grams multiplied by 100.

$$\text{Organ body weight ratio} = \frac{\text{organ weight}}{\text{body weight}} \times 100$$

7- Histopathological Studies:

Tissue specimens from liver and intestine of experimental birds of each group chicks were fixed in 10% neutral formalin solution and the specimens were routinely processed in paraffin embedding method ,sectioned and stained with Haematoxylin and Eosin (H&E) for light microscopic examination according to [26].

8- Experimental design:

Three hundred and sixty one old day broiler chick divided into 9 equal groups; 40 chicks in each (table 1) . All chick groups were reared under field condition and given ration and water. Groups 2-8 were infected with *E.coli*, groups 2,3,4 and 6 were treated with tylosine antibiotic (Tylox ®), group 2 and 8 treated with colistine sulphate, groups 4 and 5 received lysozymes while groups 6 and 7 received Betain. Groups 1 and 9 kept as negative and positive control; respectively. Average body weight (ABW), organ body weight (liver, intestine, Gizzard and Bursa) to calculate organ body weight ratio at 3rd, 7th and 10th days post infection. Average weekly feed intake was also recorded to calculate feed conversion rate (FCR). Tissue samples including liver and intestine were collected for histopathological examination.

Table (1): Treatment of chicken groups infected with *E.coli*.

Group	Infection with E.coli	Type of treatment
1	-ve	-ve
2	+ve	Tylosine + colistinne
3	+ve	Tylosine
4	+ve	Tylosine + lysozyme
5	-ve	Lysozyme only
6	+ve	Tylosine + Betain
7	+ve	Betain only
8	+ve	Colistine only
9	+ve	- ve

Results and Discussion

Avian pathogenic *E.coli* is the causative agent for Colibacillosis , the most significant infectious bacterial disease of poultry worldwide. Several pathological signs due to infection with an *E. coli* strain are recorded in broiler mainly results in respiratory infections (airsacculitis) and peritonitis/pericarditis and omphalitis/yolk sac infection. Many antibiotics are used for treatment of APEC with variable sensitivity, on the other hand antibiotic-resistant strains of *E. coli* isolated from poultry has complicated the problem[27,28] resulting in treatment failure, more over antibiotic residues in broiler meat affect human health give rise for persistence need for safe alternative such as prebiotics. Therefore our experiment is designed in order to study the beneficial effect of commercial prebiotics that used in Egyptian field against APEC and compare it with commonly used antibiotics colistine and tylosine.

Results of FCR (Table 2) revealed that best FCR was group(6) received tylosine and betain which was 1.44 followed by group (7) which received betain alone which was 1.46 then followed by group (5) which received lysozyme alone which was 1.49 then followed by group (2) which received tylosine and colistine and group (4) which received tylosine and lysozme which showed similar result 1.50 followed by group(3) received tylosine which was 1.51 then control negative group (1) which was 1.53 then the highest was control positive group infected with *E.coli* which was 1.72. Highest FCR in group 9 infected with *E.coli* may be due to negative impact of APEC *E.coli* on performance parameter, similar results were found by [29], while best FCR were those groups received betaine including groups 6 (betain and tylosine) and 7 (betaine) successively, inspit of that several researchers stated that betaine supplementation has no effect on animal performance since several years [30,31,32] recently it was found that it improves body weight of broiler chickens due to its role on improvement of Villi height, crypt depth and villi height to crypt depth ratio (v/c) of broiler chickens [19], other suggest that at an appropriate dose, betaine may spare some quantity of dl-methionine and dietary energy to support the growth process of heat-stressed broilers [20]. Our finding also revealed that lysozyme improves FCR this may due to that addition of exogenous lysozyme significantly reduced the concentration of *C. perfringens* in the ileum and the intestinal lesion scores, inhibited the overgrowth of E. coli and Lactobacillus in the ileum and intestinal bacteria

translocation to the spleen, and improved intestinal lysozyme activity in the duodenum and consequently the FCR of chickens[33], this results assisted recently by [34] who stated that exogenous lysozymes improves body weight gain of broilers chickens together with reducing number of *E. coli* in the ileum compared with feeding antibiotic to birds.

Organ BWR in the 10th days post challenge (Table 3) it was found that highest spleen body weight ratio was gr 7 received betaine which was 0.15, followed by gr 6 (tylosine and betaine) and gr 5 (lysozyme) which both have similar results 0.13, followed by gr 4 (tylosine + lysozyme) which was 0.12, then groups 8 (colistine), gr 9 control positive and gr 2 (tylosine + colistine) has similar results which was 0.11, finally gr 1 (control negative) which is 0.07. These findings suggest that groups received prebiotics has superior spleen body weight ratio with better performance than other groups .

Table (2): Performance of treated *E.coli* infected broiler chicken groups

Group Number	Age/week	Treatment	Infection	ABW	AFI	FCR
1	1	non	non	255	180	0.70
	2			530	570	1.07
	3			922.5	1160	1.25
	4			1530	2220	1.45
	5			2095	3210	1.53
2	1	Tylosine + colistin	+	247	163	0.65
	2			507.5	575	1.13
	3			889.5	1006	1.13
	4			1430	2005	1.40
	5			1952.5	2929	1.50
3	1	Tylosine	+	254	195	0.76
	2			459	589	1.28
	3			895	1102	1.23
	4			1403,5	1979	1.41
	5			1941	2950	1.51
4	1	Tylosine + Lysozome	+	241.5	198	0.81
	2			489.5	517	1.05
	3			886.5	1162	1.31
	4			1330	1950	1.46
	5			1919	2890	1.50
5	1	Lysozome	+	255.5	188	0.73
	2			513	639	1.24
	3			907	1298.5	1.43
	4			1390	2010.5	1.44
	5			1908	2850	1.49
6	1	Tylosine + Betain	+	260	196	0.75
	2			454	651	1.43
	3			904	1251	1.38
	4			1436	2139	1.48
	5			2073	3000	1.44
7	1	Betain	+	196	186	0.94
	2			475	593	1.24
	3			881	1218	1.38
	4			1430	2100	1.46
	5			1980	2900	1.46
8	1	colistin	+	268	188	0.70
	2			468	669	1.42
	3			879	1265.5	1.43
	4			1380	2050	1.48
	5			1940	2940	1.51
9	1	non	+	240	188	0.78
	2			417.5	639	1.53
	3			888	1238.5	1.39
	4			1355	2343.5	1.72
	5			1930	3325.5	1.72

Liver BWR by 10th days post challenge the highest was group 7 (betain) which was 4.09, followed by gr 6 (tylosine+betaine) which was 3.87, followed by gr 5 (lysozyme) which was 3.81, followed by gr 4 (tylosine+lysozyme) which was 3.79, followed by gr 2 (tylosine – colistine) which was 3.75, followed by control negative group 1 which was 3.50, followed by control positive group 9 which was 3.45, followed by gr 3 (tylosine) which was 2.99, followed by gr 8 (colistine) which was 2.09.this findings revealed that betain groups has highest liver BWR as it was expected that the dietary supplementation of betaine would influence carcass and parts weights due to its methyl-group donor property, which would increase methionine and cystine [35], as well as glycine for protein synthesis and also contribute to reduce fat deposition in the carcass through several metabolic routes [36].

Intestine APEC by 10th days post infection the highest was gr 4 (tylosine+ lysozyme) which was 7.19 , followed by gr 2 (tylosine + colistine) which was 6.66, followed by group 5 (lysozyme) which was 6.24 , then group 7 (betaine) which was 6.20 , followed by group 6 (tylosine – betaine)which was 6.12, then gr 3 (tylosine) which was 6.10, followed by gr 8 (colistine) which was 5.96, followed by group 9 (control positive) which was 5.83, and finally gr 1 (control negative) which was 5.60. This finding revealed that lysozymes and antibiotics have higher intestinal body weight ratio compared to control negative groups this maybe due to antibacterial effect of lysozymes which decrease intestinal destruction induced by pathogenic microorganism [22] without any huzzard effects that induced by antibiotics, tylosine also has a great role on *C. perfringens* control as this anaerobic microorganism could distruct intestinal mucosa especially in presence of environmental stress and affect normal organ growth [37]**,** inspite of some researcher reported that colistine sulphate gain either sensitive, intermediary and resistant susceptibility against APEC [38], in contrast other researcher pointed that colistine sulphate considered the lowest resistant antibiotic against avian pathogenic *E.coli* APEC [39] which resulting in better intestinal health and growth after controlling invasive microorganisms also our finding ensure the beneficial effect of betaine on intestinal body ratio when compared with control negative group this maybe due to it improve villi height, crypt depth and villi height to crypt depth ratio (v/c) of broiler chickens lead to better intestinal health [19].

Gizzared –proventriculus BWR it was found by 10th days post infection that highest ratio was gr 4 which was 4.47 followed by gr 2 which was 4.16 followed by gr 3 which was 4.07 followed by gr 5 which was 4.04, followed by gr 8 which was 3.66, followed by groups 6 and gr 7 which showing same results 3.65, then followed by gr 1 (control negative) which was 3.60 and finally gr 9 which was 3.57. Our results assist the fact of beneficial antimicrobile effect of lysozyme that helps in better performance either in combination with antibiotics or alone, higher gizzared-proventriculus BWR of betaine group either alone or combined with tylosine compared to control negative group support fact of beneficial effect of betaine on internal organs as it can play the role of an osmolyte via apply an osmoprotective effect by accumulating in cell organelles and cells exposed to osmotic and ionic stress specially under high ambient temperature [40,20].

Average body Table (3): Average body (ABW) and mean organ body weight/ gm (mw) as well as organ body weight ratio (OBR) at in E. coli infected treated chickens.

Gr No	Treatment	Infection	DPI	ABW	spleen		Liver		Intestine		Gizzard+pro.		Bursa	
					mw	OBR	mw	OBR	mw	OBR	mw	OBR	mw	OBR
1	Negative control		3	613	0.45	0.07	18	2.93	49	7.99	30.5	4.97	1.34	0.21
			7	778	0.51	0.06	40	5.14	53	6.81	29	3.72	0.9	0.11
			10	1000	0.7	0.07	35	3.5	56	5.6	36	3.6	1.5	0.15
2	Tylosine + colistin	+	3	575	0.36	0.06	22	3.82	53	9.21	27	4.69	1.14	0.19
			7	653	0.72	0.11	23	3.52	42	6.43	28	4.28	0.95	0.14
			10	720	0.8	0.11	27	3.75	48	6.66	30	4.16	1.2	0.16
3	Tylosine	+	3	630	0.59	0.09	17.5	2.77	45.6	7.23	23.5	3.73	1.12	0.17
			7	818	1.41	0.17	25	3.05	49	5.99	44	5.37	1.30	0.15
			10	835	0.9	0.10	25	2.99	51	6.10	34	4.07	1.5	0.17
4	Tylosine + lysozyme	+	3	480	0.42	0.08	14.3	2.97	33.8	7.04	21.2	4.41	0.79	0.16
			7	633	0.85	0.13	26.5	4.18	41	6.47	50	7.89	0.9	0.14
			10	737	0.89	0.12	28	3.79	53	7.19	33	4.47	1.4	0.18
5	Lysozyme	+	3	627	0.51	0.08	22	3.50	38.8	6.18	29.5	4.70	0.99	0.15
			7	823	0.68	0.08	29	3.52	45	5.46	41	4.98	1.1	0.13
			10	865	1.3	0.13	33	3.81	54	6.24	35	4.04	1.5	0.17
6	Tylosine + Betain	+	3	557	0.64	0.11	20.5	3.68	47.4	8.50	24.2	4.34	0.93	0.16
			7	773	1.2	0.15	24.5	3.16	52	6.72	52	6.72	1.6	0.20
			10	930	1.3	0.13	36	3.87	57	6.12	34	3.65	1.9	0.20
7	Betain	+	3	635	0.41	0.06	21.5	3.38	52.7	8.29	29	4.56	0.90	0.14
			7	855	0.95	0.11	36	4.21	48	5.61	47	5.49	1.7	0.19
			10	903	1.4	0.15	37	4.09	56	6.20	33	3.65	1.9	0.21
8	Colistin	+	3	645	0.62	0.09	25	3.87	53.8	8.34	30.1	4.66	1.4	0.21
			7	768	0.45	0.05	30	3.90	53	6.90	52	6.77	1.2	0.15
			10	955	1.1	0.11	20	2.09	57	5.96	35	3.66	1.8	0.18
9	Infected non treated		3	589	0.42	0.07	23	3.90	33	5.6	28.5	4.83	0.8	0.13
			7	635	0.6	0.09	28.9	4.55	48	6.14	27	4.25	1.0	0.15
			10	840	1.0	0.11	29	3.45	49	5.83	30	3.57	1.4	0.16

Liver stained sections of *E. coli* infected treated chickens (H&E X 200).

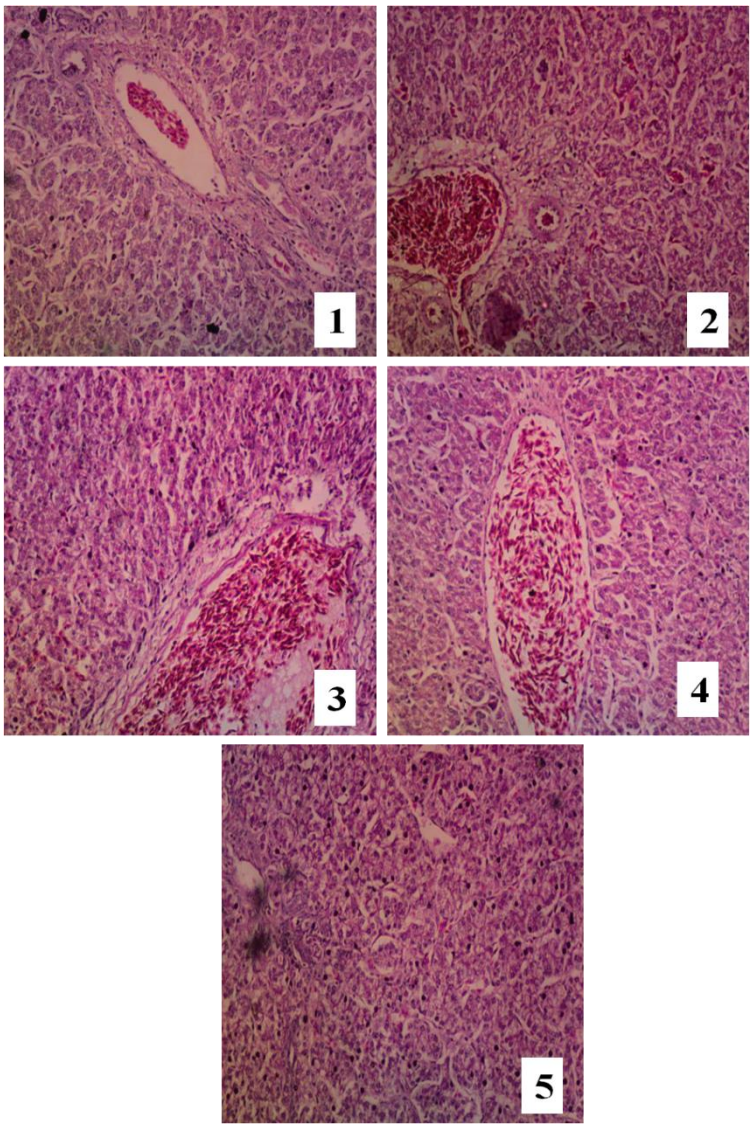

Fig (1): Chicken liver showed mild congestion of the portal vein.
Fig (2): Chicken liver showing severe congestion of the portal vein and sinusoids the hepatocytes suffering from vacuolar degeneration in the cytoplasm with disorganization of the hepatic cord.
Fig. (3): Chicken liver showing congestion of the portal vein.
Fig (4): Chicken liver showing congestion of the central vein.
Fig (5): Chicken liver group 5 showing vacuolar degeneration in the hepatocytes cytoplasm.

Intestine stained sections of *E. coli* infected treated chickens (H&E X 200).

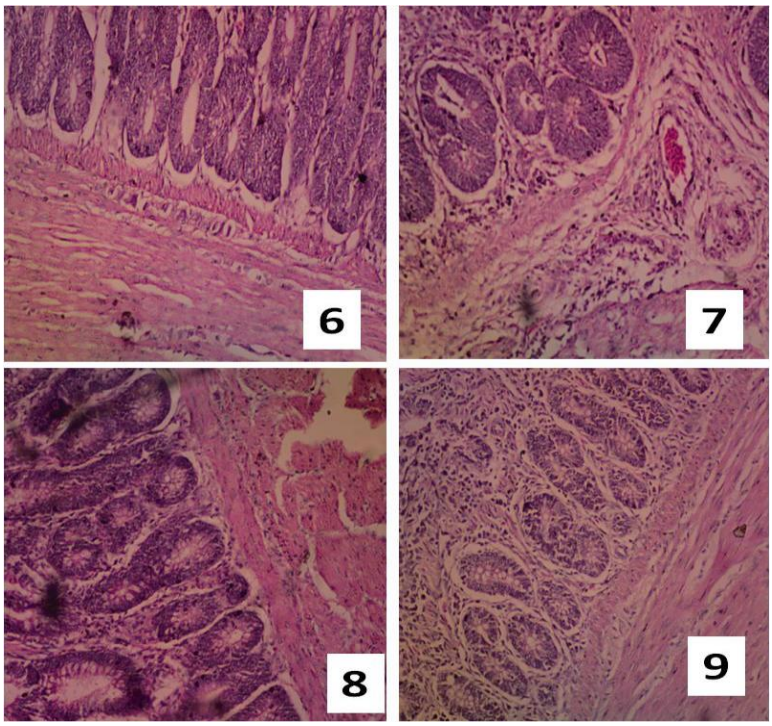

Fig (1) Chicken intestine group 2 normal.
Fig.(2) Chicken intestine gr 9 showing severe congestion of the blood vessels in the sub mucosa accompanied with mild edema with inflammatory cells inflation in both the mucosa and the sub mucos.
Fig .(3) : Chicken intestine showing mild inflammatory cells infiltration of the mucosa.
Fig (4): Chicken intestine showing inflammatory cells infiltration of the mucosa.

Bursal body weight ratio by the 10th days post infection the highest was group 7 (betaine group) which was 0.21, followed by group 6 (tylosine- betaine group) which was 0.20, followed by group 4 (tylosine-lysozyme) and group 8 (colistine group) which show similar results 0.18, followed by group 3 (tylosine group) and group 5 (lysozyme group) which also show similar results 0.17, then groups 2 (tylosine-colistine) and group 9 (control positive infected with APEC) are showing similar results which was 0.16, finally group 1 (control negative)which was 0.15. this findings was matched with results found by these results are matched with the findings of [41,16] who suggested that betaine promoted immune system of broiler chickens. Similar results was found by [19] who stated that betaine improves bursal body weight ratio when compared with control negative groups.

Histopatholgical finding of liver are varied from group to another as group one shows no histopathological changes while gr 2,6,7 and 8 showed mild changes after challenge in form of mild congestion of portal vein (fig. 1) on the other hand control positive group 9 showed severe congestion of the portal vein and sinusoids the hepatocytes suffering from vacuolar degeneration in the cytoplasm with disorganization of the hepatic cord (fig. 2), groups 3,4 and 5almost showed the same lesion in the form of congestion of the portal vein (fig. 3), congestion of the central vein (fig 4) and vacuolar degeneration of hepatocyte (fig 5) which considered a reversible condition. Our result cleared that avian pathogenic *E.coli* (APEC) induced pathological change in the liver of infected control positive while on the other hand groups treated with antibiotic combination tylosine-colistine control the infection thus prevent pathological changes occurs in liver, this results was matched with [42] who reported that *E.coli* s sensitive to colistine sulphate and it was the most sensitive antibiotic with lowest resistance (3%) among tested antibiotic, betaine has cellular protective effect that protect hepatic cell from pathological changes induced by pathogenic bacteria especially in hot weather, this results was matched with [43] who stated that betaine provides antioxidant capacity for attenuating the hepatocyte necrosis by CCl4, and so considered a potent nutritional or therapeutic factor for reducing liver fibrosis. Also lysozyme may has antibacterial effect on *E.coli* resulting in decrease its population and decrease its infective dose, this results was found by [34] who reported that lysozyme reducing number of *E.*

coli in the ileum compared with feeding antibiotic to birds. Concerning histopathological finding of intestine, group (1) control negative group showing no lesions and normal histopathological section as shown in fig.(6), while gr (9) control positive showing severe congestion of the blood vessels in the sub mucosa accompanied with mild edema with inflammatory cells inflation in both the mucosa and the sub mucosa, while chickens groups 2,4,5 and 8 showing mild inflammatory cell infiltration as shown in fig (8), while groups 3,6 and 7 showing inflammation with inflammatory cell infiltration in mucosa and submucosal layer as shown in fig (9).this results revealed that antibiotic colistine and lysozymes control *E.coli* and prevent destructive effect on intestinal mucosa, this was parallel with results found by [39] who reprted that colistine sulphate showing highest sensitivity against *E.coli* thus control infection and pathological changes induced by this pathogenic microorganism, also [22] stated that lysozyme has antibacterial effect which decrease intestinal destruction induced by pathogenic microorganism, moreover [34] reported that lysozymes decrease population of APEC in the intestine thus maybe prevent pathological changes.als betaine improve intestinal health and villi height and immune response and so dilute pathological changes induced by APEC infection[19] Finally; Comparing results of this study we noticed that administration of Colestine and/or tylosine (groups 2,3 and 8) to *E.coli* infected chicken groups showed higher performance than the control negative and infected non treated groups, and chicken given both drugs in combination were higher than those given single drug. Groups (5 and7) given periodic (Tylosine and/or Betain) showed higher results than control groups. Also combination of both prebiotic and antimicrobials showed improved results (gr 4 and 6) .

It could be concluded that antibiotics used against avian pathogenic *E.coli* still of value in control of infection by improving performance either single or in combination. The used prebiotic showed to play an important role in improving productivity of infected chickens. The used combinations are safe and effective. Therefore, we can advice to use of combination between antibacterial and prebiotic for prevention and control of infection in high risk facing poultry industry.

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