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مجلة النماء للعلوم و التكنولوجيا

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مجلة علمية محكمة تصدر عن كلية الزراعة جامعة الزيتونة

تنويه

1. المجلة ترحب بما يصل إليها من أبحاث وعلى استعداد لنشرها بعد التحكيم.
2. المجلة تحترم آراء المحكمين وتعمل بمقتضاها.
3. كافة الآراء والأفكار المنشورة تعبر عن آراء أصحابها فقط.
4. يتحمل الباحث مسؤولية الأمانة العلمية وهو المسؤول عما ينشر عنه.
5. البحوث المقدمة للنشر لا ترد لأصحابها سواءً نشرت أو لم تنشر.

مجلة النماء للعلوم والتكنولوجيا

السنة الرابعة العدد الرابع المجلد (1) مارس 2023

مجلة علمية محكمة - تصدر دورية سنوية - عن كلية الزراعة جامعة الزيتونة

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مجلة النماء للعلوم والتكنولوجيا: مجلة علمية دورية محكمة تصدر عن كلية الزراعة جامعة الزيتونة تعنى بالبحوث والدراسات المبتكرة في مختلف العلوم التطبيقية وتقبل نشر الأبحاث العلمية الأصيلة والنتائج العلمية المبتكرة.

الرسالة

الاسهام في نشر العلوم والمعارف الحديثة باستخدام أحدث معايير وتقنيات النشر والطباعة، ودعم الإبداع الفكري والتوظيف الأمثل للتقنية والشراكة المحلية والعالمية الفاعلة.

الرؤيـة

الارتقاء بإصدارات المجلة لتصبح مصادر معرفة ذات قيمة علمية تفيد المجتمع، والريادة العالمية والتميز في نشر البحوث العلمية.

الأهداف

1- تحقيق تقدم في التصنيفات العالمية عن طريق تقوية الجامعة بأكملها، والتميز بحثياً وتعليمياً في كافة المجالات.

2- استقطاب وتطوير أعضاء هيئة تحكيم واستشاريين متميزون.

3- تحقيق الجودة المطلوبة للبحث العلمي.

4- تمكين الباحثين والمحكمين من اكتساب المهارات الفكرية والمهنية أثناء حياتهم البحثية والعلمية.

5- بناء جسور التواصل داخل الجامعة وخارجها مع الجامعات الأخرى المحلية والإقليمية والعالمية.

قواعد النشر

تصدر المجلة وفق مبادئ الدين الإسلامي الحنيف، ووفق قوانين الإصدار للدولة الليبية، وكذلك وفق رؤية ورسالة وأهداف جامعة الزيتونة.

قواعد و شروط النشر بمجلة النماء للعلوم و التكنولوجيا كلية الزراعة جامعة الزيتونة

1- أن يكون البحث لم يسبق نشره في أي جهة أخرى وأن يتعهد الباحث كتابة بذلك.

2- أن يكون البحث مكتوباً بلغة سليمة، ومراعياً لقواعد الضبط ودقة الرسوم والأشكال إن وجدت، ومطبوعاً بخط (Simplified Arabic) للغة العربية، وبخط (Times News Roman) للغة الأجنبية، وبحجم (12)، وبمسافة مفردة بين الأسطر، وأن تكون أبعاد الهوامش للصفحة من أعلى وأسفل (4 سم) ومن الجانبين (3 سم)، وألا يزيد البحث عن (25) صفحة.

3- أن تكون الجداول والأشكال مدرجة في أماكنها الصحيحة، وأن تشمل العناوين والبيانات الايضاحية الضرورية، ويراعى ألا تتجاوز أبعاد الأشكال و الجداول حجم حيز الكتابة في صفحة Microsoft Word.

4- أن يكون البحث ملتزماً بدقة التوثيق، وحسن استخدام المراجع، وأن يراعى اتباع نظام (APA) في توثيق المراجع داخل النص وفي كتابة المراجع نهاية البحث.

5- تحتفظ المجلة بحقها في اخراج البحث وإبراز عناوينه بما يتناسب واسلوبها في النشر.

6- تنشر المجلة البحوث المكتوبة باللغة الأجنبية شريطة أن ترفق بملخص باللغة العربية لا يتجاوز 250 كلمة.

7- ترسل نسخة من البحث مطبوعة على ورق حجم (A4) إلى مقر المجلة، أو نسخة إلكترونية إلى البريد الالكتروني للمجلة (annamaa@azu.edu.ly)، على أن يكتب على صفحة الغلاف: اسم الباحث ثلاثي، مكان عمله، تخصصه، رقم الهاتف والبريد الإلكتروني.

8- يتم تبليغ الباحث بقرار قبول البحث أو رفضه خلال مدة أقصاها ستون يوماً من تاريخ استلام البحث، وفي حالة الرفض فالمجلة غير ملزمة بذكر أسباب عدم القبول.

9- في حالة ورود ملاحظات وتعديلات على البحث من المحكم يتم ارسالها للباحث لإجراء التعديلات المطلوبة وعليه الالتزام بها، على أن يعاد إرسالها للمجلة خلال فترة أقصاها خمسة عشر يوماً.

10- أن يلتزم الباحث بعدم إرسال بحثه لأية جهة أخرى للنشر حتى يتم اخطاره برد المجلة.

11- دفع الرسوم المخصصة للتحكيم العلمي وللمراجعة اللغوية والنشر، إن وجدت.

كلمة افتتاحية

الحمد لله حمداً كثيراً طيباً مباركاً فيه، والصلاة والسلام على محمد وعلى آله وصحبه أجمعين.

يسعد أسرة مجلة النماء للعلوم والتكنولوجيا أن تقدم للباحثين أصدق التحيات وأعطرها بعد إصدارها بشكل منتظم وردود الفعل التي تلقيناها والتي كانت لنا بمثابة دافع لمواصلة السير قدماً، لتطوير بيت الخبرة، لكي يكون استمراراً للجهود المبذولة وتوثيق النتاج العلمي الأكاديمي المتخصص، رغبة من هيئة التحرير في أن تكون المجلة منفذاً لنشر الإنتاج العلمي الذي سيقدم في المجالس العلمية، ولجان الترقية، وفقاً للقواعد والضوابط المنصوص عليها.

فمن خلال العدد **الرابع المجلد الأول مارس 2023م** نهديكم أعزاءنا القراء والبحاث عدداً من البحوث والدراسات في مجالات متنوعة والتي تشكل حلقة مهمة في السلسلة البحثية لتعميق المعرفة لديكم ودعم مصادركم.

وفي الختام نتقدم بالشكر والامتنان إلى كل من ساهم وعمل على استمرار هذه المجلة العلمية، وندعو جميع الباحثين المهتمين بالعلوم والتكنولوجيا إلى تقديم نتاجهم العلمي للنشر فيها.

أسرة المجلة

المحتويات

مجلة النماء للعلوم والتكنولوجيا (STDJ)
السنة الرابعة العدد الرابع المجلد (1) مارس 2023
مجلة علمية محكمة تصدر عن كلية الزراعة جامعة الزيتونة

المحتويات

An updated review on poultry coccidiosis

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دراسة مرجعية حديثة عن كوكسيديا الدواجن

فتحي منصور علي أبوحجر
قسم الأحياء، كلية التربية، الجامعة الأسمرية الإسلامية، زليتن، ليبيا

الملخص:

الكوكسيديا مرض شائع ومهم تجاريًا تسببه طفيليات من جنس Eimeria. تم اكتشاف المرض في العديد من المواقع في جميع أنحاء العالم، وتأثيره الاقتصادي على قطاع الزراعة الحيوانية كبير. تم تحقيق السيطرة على الكوكسيديا في الدجاج باستخدام الكوكسيديا الحية أو العقاقير المضادة للفطريات في العلف. ومع ذلك، يستمر تفشي انتشار الكوكسيديا بين الدواجن، وتنتشر العدوى تحت الإكلينيكية، التي تؤثر بشكل كبير على الإنتاجية والأمن الغذائي بسبب المقاومة الواسعة للأدوية وانتشار الطفيليات والمثابرة البيئية. نقترح العديد من الحلول لمعالجة هذه المشكلة، نظراً لإمكاناتها الاقتصادية الهائلة، فإن صناعة الإضافات العلفية تبحث بشكل مكثف عن المنتجات المستقبلية التي تعزز صحة الأمعاء وتقي من الأمراض المعوية، وكذلك التدابير البديلة الأخرى. تناولت الدراسة المواضيع التالية: الأهمية الاقتصادية، الكوكسيديا في إنتاج الدواجن، وميكروبات الأمعاء.

الكلمات المفتاحية: *الكوكسيديا، الإضافات العلفية، تدابير بديلة، ميكروبات الأمعاء*

Abstract:

Coccidiosis is a common and commercially important poultry disease caused by protozoan parasites of the genus *Eimeria*. The disease is found in many locations worldwide, and its economic impact on the animal agriculture sector is significant. Control of coccidiosis in chickens was achieved with the use of live coccidia or in-feed anticoccidial drugs. However, coccidiosis outbreaks continue to occur, and subclinical infections, which significantly impact productivity and food security, are ubiquitous because of broad medication resistance, parasite prevalence, and environmental persistence. We propose many solutions to address this issue, Due to its enormous economic potential, the feed additive industry has been intensively researching future products that enhance intestinal health and prevent intestinal diseases, and other alternative measures. The study addressed the following topics: economic importance, coccidiosis in poultry production, and gut microbiota.

Keywords: *Coccidiosis; anticoccidials; alternative measures; gut microbiota.*

Introduction:

Coccidiosis in chickens cost the global economy an estimated £10.36 billion in 2016, including lost productivity and prevention and treatment costs (Blake, et al.,2020). Besides increasing the incidence of *Clostridium perfringens* and *Salmonella enterica* serovars Typhimurium and Enteritidis in the intestine, coccidiosis increases the risk of animal foodborne infections (Blake, & Tomley, 2014). Coccidiosis causes the breakdown of intestinal epithelial cells and triggers an immune response in the host, resulting in increased maintenance costs, reduced food absorption, and ultimately reduced chicken development (Lee, & Lillehoj, 2022). The chicken sector has developed a variety of management strategies to protect against the pathogenicity of *Eimeria* and the adverse effects of coccidiosis. Of these approaches, chemotherapeutic agents or anticoccidial drugs are the most effective, besides vaccination initiatives (Chapman, 2014). Importantly, after the drugs were found, a change in *Eimeria* sensitivity to anticoccidial drugs was observed, and evidence of worldwide coccidial resistance to anticoccidial drugs has been established. Over the past decade, there has been increased public concern about microbial resistance to control measures and their implications for human healthb (Cosby, et al.,2015). The likelihood that new, more effective antibiotics to combat *Eimeria* parasite will be developed in the future has decreased. The chicken sector is transitioning to an antibiotic-free era because of consumer and regulatory pressure, nutritional interventions, and finding alternatives to antibiotics and anticoccidial drugs that do not affect growth performance have become critical.The first ten days of a chick's life are spent building the digestive and immunological systems. Broiler chickens spend more time on immature guts and immune systems as the time to market shortens. Pathogens can also harm a chicken, halting its development and redirecting resources to repair damaged intestines. This is especially true of the parasite *Eimeria*, which causes coccidiosis by attacking the gut. In the poultry sector, many alternatives aim to preserve the growth and health of the birds while enhancing their overall performance (Gadde, et al., 2017). The switch from anticoccidial agents to *Eimeria* vaccines has heightened the importance of gut health in birds because of concerns about antibiotics and resistance. Given the time required for vaccination to produce adequate protection, we should examine dietary measures to assist chicks in developing gut and immune systems. We have proposed natural products as one option. A previous study has observed the anti-inflammatory and protective effects of chitosan against *E. papillata* -infection in mice. However, compared to chitosan-rEm14-3-3 NPs and rEm14-3-3, poly (D, L-lactide-co-glycolide) -rEm14-3-3 NP-vaccinated chicken dramatically reduced relative body weight gain, lowered lesion score, and improved oocyst reduction ratio in chicken challenged with *E. maxima* (Haseeb, et al., 2022). In addition, we discussed the economic significance of coccidiosis in chicken production and gut microbiota.

1.Economic importance

Coccidiosis is a serious economic concern in the poultry sector. Between 1961 and 2019, global poultry meat output increased from 9 to 132 million tonnes, while egg production increased from 15 to 90 million tonnes (FAO). Imports of chicken meat (excluding paw) are expected to reach 800,000 metric tons (MT) in 2022, up 2% from 2021 levels. Chicken meat production is predicted to decrease by 3% in 2022 because of the reduced output of yellow-feathered broilers. The production of white feather broilers is expected to remain stable beginning in 2021, according to USDA data 2022. This increasing demand for meat is because of the world's expanding population and purchasing power, and chicken meat is less expensive than other varieties of meat. Although the global supply of meat has expanded, there are still obstacles impeding the industry's success, such as bird handling, housing, raising, and disease prevention (nutritional, metabolic, and parasitic diseases) (Nahed, et al., 2022). Coccidiosis in chickens is projected to have cost the world economy £10.36 billion in 2016, including productivity losses and expenditures associated with prevention and treatment (Blake, et al.,2020). Coccidiosis contributes to additional loss and concerns about zoonotic food-borne diseases by increasing *C. perfringens* and *S. enterica* serovars Typhimurium and Enteritidis intestinal colonization (Blake, & Tomley, 2014).

2.Coccidiosis in poultry production

Coccidiosis in poultry is caused by many *Eimeria* species, which are classified as protozoa in the phylum Apicomplexa. Apicomplexan parasites, such as *Cryptosporidium*, *Toxoplasma*, *Sarcocystis*, and *Eimeria* have been identified (Wasmuth, et al.,2009). *Eimeria* is a parasitic protozoan that dwells in the epithelial cells of the intestines of vertebrates, including horses, domestic dogs, cats, rabbits, cattle, sheep, pigs, turkeys, and chickens. Scientists have found that the chicken has many varieties of *Eimeria*, including *Eimeria acervulina, Eimeria brunetti, Eimeria maxima, Eimeria mitis, Eimeria necatrix, Eimeria praecox,* and *Eimeria mivati.* They are the main source of chicken coccidiosis, a disease that causes sporulation and financial losses in animal industries, particularly poultry, because of intense rearing conditions. In domestic chickens (*Gallus gallus domesticus*), seven *Eimeria* species prefer the ceca and gut. Cecal coccidiosis is caused by *E. tenella*, while other species cause intestinal coccidiosis. *E. maxima*, *E. acervulina*,*E. tenella*, and *E. necatrix* are recognized to pose significant problems in the poultry business because of their ubiquity, pathogenicity, and immunological features. *Eimeria* has been found to infect a wide range of vertebrate hosts, including pigs, horses, goats, dogs, rabbits, turkeys, and chickens. *Eimeria necatrix*, *Eimeria tenella*, *Eimeria maxima*, and *Eimeria brunetti* are the most pathogenic species, while *Eimeria mitis* and *Eimeria acervulina* are the least harmful. Variables affecting the clinical outcome of coccidial infections include the age and nutrition of the birds, the efficacy of preventive anticoccidial medicines, interfering illnesses, and stress. Many *Eimeria* species may infect a single vertebrate host. A recent study has shown different immunological responses to *E. tenella* infection in genetically diverse chicken lineages (Lee, et al.,2016). Intensive raising conditions, anticoccidial feed additives, and vaccination all exerted selection pressure on *Eimeria* species, leading to the emergence of not just immunologically different species but also strains. After investigating the immunogenicity of *E. maxima*, Rose and Long determined that it is the most immunogenic species of avian coccidia (Blake, et al.,2020). Because of the immunological diversity of *E. maxima* strains, live vaccines may not protect birds against infections with heterologous strains. Recently, more sophisticated molecular techniques have been used to characterize these inter- and intraspecies variations, such as amplified fragment length polymorphisms (AFLP). The examination of these distinctions led to the identification of several strain-specific immunoprotective antigens (Blake, et al.,2011). Due to the regional variability of coccidial strain antigenicity, there is a possibility of introducing undesirable *Eimeria* species into the environment (Wasmuth, et al.,2009). Immune responses to *Eimeria* spp. are confounded by exogenous (in-the-environment) and endogenous (inside- the- host) developmental stages throughout the life cycle (Rose, & Hesketh,1987). The antigenic stimulation magnitude, the life stage, and the antigen composition of various phases all affect the responses. Asexual schizonts are more immunogenic than sexual gamonts (Figure 1).

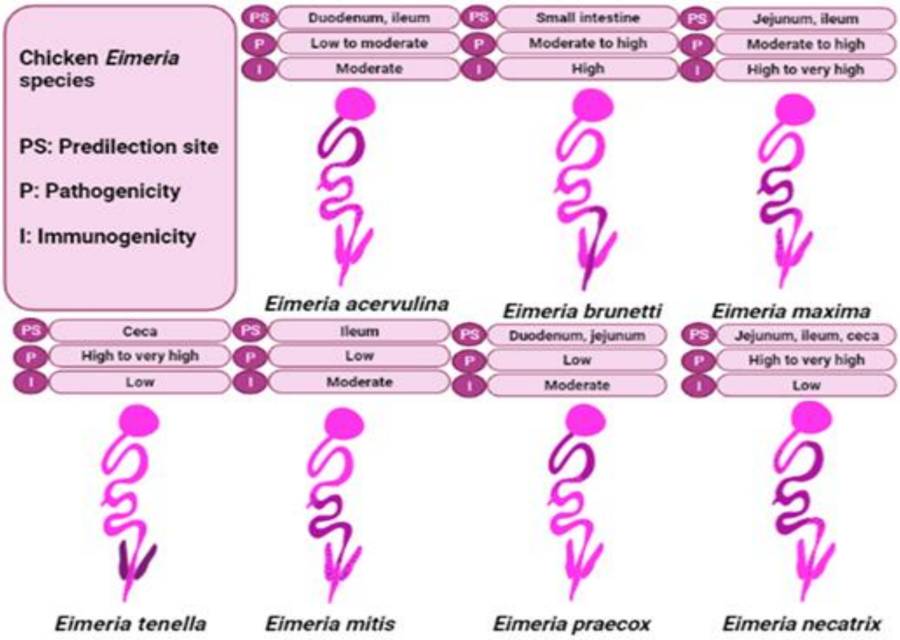

Figure 1. The predilection site, pathogenicity, and immunogenicity of seven parasite *Eimeria* species in chickens.

2.1 Life cycle

Eimeria species are monoxenous parasites (infecting just one host), with a normal coccidian life cycle comprising exogenous and endogenous developmental stages(Figure 2). *Eimeria*'s life cycle is complex. However, it may be divided into three stages: sporogony, schizogony, and gametogony. An unsporulated oocyst is an exogenous stage that is excreted in the feces. The environmentally tolerant oocysts may sporulate in the presence of oxygen, humidity, and an ideal temperature. The one-celled sporont of an unsporulated oocyst may undergo meiotic and mitotic divisions to generate a sporulated oocyst with four sporocysts, each with two sporozoites. The grinding gizzard mechanically disrupted the sporulated oocysts after being consumed by the vertebrate host. Sporozoites excyst from the released sporocysts under the influence of pancreatic enzymes and bile salts. *Eimeria* species have evolved to the point where they may infiltrate intestinal epithelial cells from the duodenum to the cecal pouches. Thus, *Eimeria* spp. are not only host and location-specific but also tissue-specific. Free sporozoites infiltrate intestinal epithelial cells (IECs) and intestinal intraepithelial lymphocytes (IELs). IELs are utilized as a translocation vehicle for trophozoites to get to the preferred locations (the crypt), where they go through a set number of merogonic cycles (typically two to five) before being differentiated into male and female gametocytes. (Rose, & Hesketh,1987). After sexual replication, the zygote is produced, and eosinophilic granules move to the periphery and degranulate to shape the oocyst wall. Unsporulated oocysts are expelled in feces and subsequently sporulate in a moist, oxygen-rich environment.

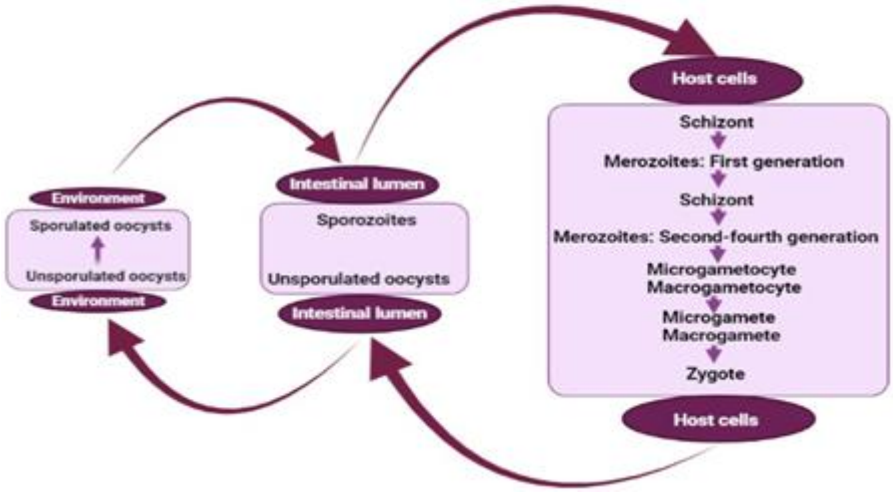

Figure 2. *Eimeria* life cycle diagram.

Eimeria oocysts may be divided into three categories based on their size: large (*E. maxima*), medium (*E. necatrix and E. tenella*), and small (*E. acervulina*). However, *E. brunetti* and *E. praecox* have oocysts that are medium to large. *E. acervulina*, *E. tenella*, and *E. maxima* are common in short-lived birds. We can classify these oocysts as small, medium, or large (Figure 3) (Nahed, et al.,2022).

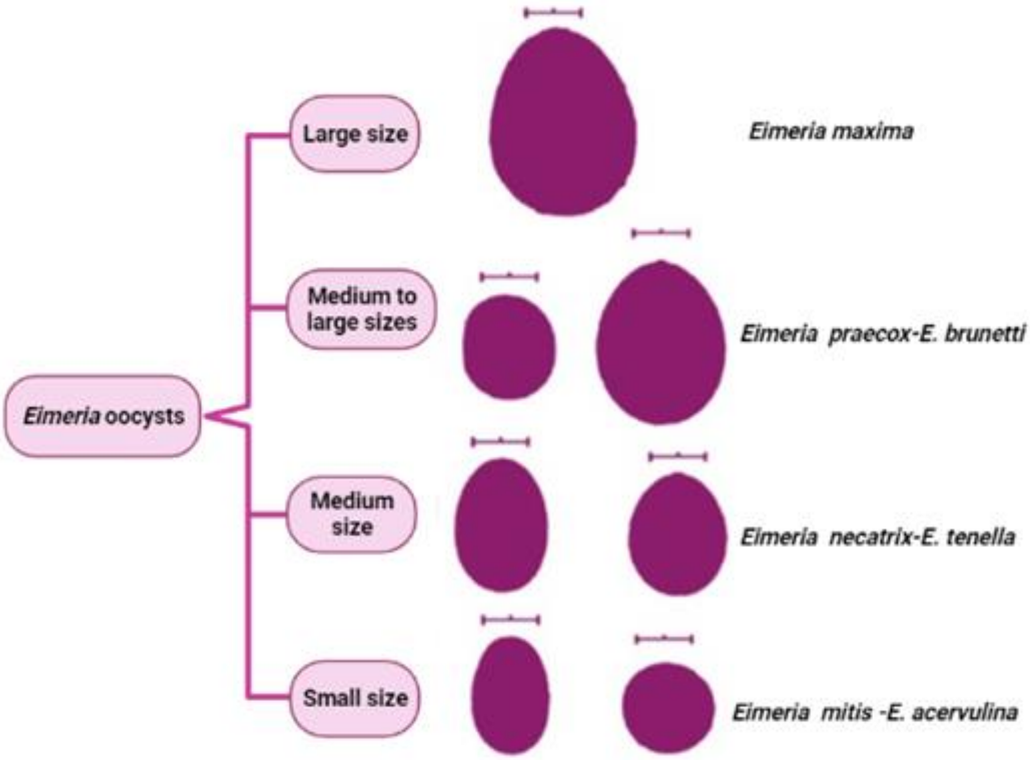

Figure 3. Categories of *Eimeria* oocysts based on their size.

3. Control measures
3.1 Alternatives strategies

Recently, consumers have expressed growing concern about the potential emergence of antibiotic-resistant bacteria due to overuse and underuse of antibiotics in livestock. As a result, several antibiotics have been banned from animal feed worldwide. Currently, alternatives have been researched more intensely as the broiler sector has declined and the use of antimicrobials has been eliminated (Diarra, & Malouin,2014). Due to its enormous economic potential, the feed additive industry has been intensively researching future products that enhance intestinal health and prevent intestinal diseases. Some of these products have been proven to be useful in the prevention of coccidiosis alone, while others have been found to be effective in conjunction with immunization. In the poultry industry, many options have been proposed to maintain optimal growth performance while improving the bird's overall health. Probiotics, prebiotics, synbiotics, organic acids, enzymes, fats, minerals, proteins, and amino acids, and phytogenic feed additives are some of the options that have shown varying degrees of success in treating infections caused by *Eimeria* species (Gadde, et al.,2017).

3.1.1 Organic Acids (acidifiers)

Organic acids(acidifiers) are carboxylic acids having the formula R-COOH, which are often found in plant and animal tissues (Bozkurt, et al.,2014). Acidifiers are weak acids that are administered to birds for bactericidal reasons as well as to lower the pH and digestibility of their meals. Formic acid, acetic acid, propionic acid, or butyric acid alone, and mixtures thereof, are the most commonly used acidifiers. As a replacement for zinc bacitracin, acidifier blends have been shown to diminish the effect of NE challenge on chickens, as evidenced by improved performance and health of broilers (Kumar, et al.,2022, Kumar, et al.,2021). When acetic acid was given to *E. tenella*-infected broilers, it boosted body weight gain by 14%, lowered lesion scores, and dropped cecal pH compared to unsupplemented broilers. Hydrochloric acid supplementation has similar effects. Various effects have been reported depending on the level of supplementation, with most supplementation likely to have negative effects (Cosby, et al.,2015, Mustafa, et al.,2021). By neutralizing the adverse effects of coccidial challenge, organic acid supplementation enhanced responses in a manner comparable to unchallenged controls. Maltodextrin, sodium chloride, citric acid, sodium citrate, silica, malic acid, citrus extract, and olive extract reduced *E. tenella* and *E. bovis* infections in vitro and in vivo by strategies that reduced *Eimeria* virulence and suppressed host inflammatory responses (Mustafa, et al.,2021).

3.1.2 Enzymes

Enzymes help fed animals absorb nutrients more effectively, even if they can't digest them on their own (Mansoori, et al.,2010). This is particularly useful in animals with impaired digestive and absorption functions, such as chickens with *Eimeria*. By lowering the quantity of undigested protein in the chicken hindgut, phytase prevented secondary infections, such as NE, while not affecting intestinal lesions by boosting D-xylose absorption (Mansoori, et al.,2010. Emami, et al.,2021). The inclusion of protease did not affect the performance-detrimental effect of the vaccine. however, observed better body weight gain in *E. acervulina, maxima,* or *E. tenella* -challenged chickens supplied with protease. Exogenous β-glucanase improved growth performance in coccidiosis-vaccinated broilers, acting as a partial alternative to dietary drugs (Walk, et al.,2011). Broilers' growth performance was reduced when exposed to HB, while it was enhanced by exogenous β-glucanase. However, the highest amount of exogenous -glucanase had no effect on the performance of 0–11-day-old broilers fed a 60% hulless barley-based diet. This suggests that too much β -glucanase may be bad for the early stages. Similarities in response to carbohydrase enzyme or xylooligosaccharide supplementation may indicate that carbohydrase hydrolysis products have prebiotic-like effects on 21-day-old broilers that have been fed a mixed grain diet and challenged with *Eimeria* species (Karunaratne, et al.,2021).

3.1.3 Nucleotides

Nucleotides are the basic units of nucleic acids found in all cells. It is normally found in cells as adenosine 5-triphosphate (ATP). Yeast has also been shown to be high in nucleotides when it comes to nutritional components (K Carver, et al.,1995. Sauer, et al.,2011). Nucleotides were previously considered non-essential nutrients because of the suitability of the two endogenous synthetic pathways in animals but are now regarded as semi-essential (K Carver, et al.,1995). Nucleotides are considered essential nutrients in three scenarios: inadequate intake, rapid body growth, and the existence of illnesses. Nucleotides administered at 0.04-0.07% did not affect carcass productivity or yield after 42 days. Birds fed a diet supplemented with 5 g/kg of torula yeast -produced RNA grew faster four weeks after supplementation, but the layers gave different results without affecting performance throughout the supplementation period. Torula yeast supplementation increased jejunum and ileum weight after Eimeria infection. As a result, the author concluded that the addition of nucleotides is not effective for healthy birds (Jung, & Batal,2012). Supplementation with nucleotide-rich yeast extract (YN) showed no influence on growth performance, caloric efficiency, or gut function but boosted immune organ weight regardless of Eimeria exposure. Supplement YN reduced the effects of Eimeria on villus growth and cecal pH but had a detrimental impact on villus growth in the absence of Eimeria challenge (Leung, et al.,2019).

3.1.4 Proteins and amino acids (AA)

In the management of dietary resources, it has been shown that the maintenance of body proteins, including eliminating pathological effects, is more important than physical activity, such as growth and reproduction (Coop, & Kyriazakis,1999). During pathogenic infection, protein and amino acid requirements rise because of the innate immunity, restoration of injured tissues, and the adaptive immunity development. During vaccination, increased protein content in starter diets positively affected broiler body weight, feed conversion ratio, and overall performance (Sandberg, et al.,2007). increasing coccidia-infected broiler arginine and threonine dietary supplements reduced the destruction of the intestinal mucosa and altered the immune response (Tan, et al.,2019). Arginine is required for normal lymphoid organ development. Therefore, higher arginine concentrations may help optimize immune responses or disease resistance in Eimeria-infected broilers (Jahanian,2009). By reducing TLR4 mRNA expression and activating mTOR complex 1 pathways, high doses of arginine are thought to mitigate mucosal disruption in the intestine (Tan, et al.,2019). Mucin components, including serine, cysteine, and, in particular, threonine, are important components of mucin, which is a component of the mucous layer (Montagne, et al.,2004). Better intestinal immune response to increased dietary threonine intake, which also contributed to the maintenance of normal development in Eimeria-infected broilers (Tan, et al.,2019). Increased amounts of sulfur amino acids (methionine and cysteine), arginine, and threonine in the broiler diet have also been reported to increase cell-mediated immunity and reduce the effects of coccidial infection. (Yazdanabadi, et al.,2020). Cys, Arg, Met, Ala, Tyr, and Thr appear to be most affected by Eimeria in broilers, suggesting that these AAs may be potentially limiting for Eimeria-infected broilers. As a result, dietary management of these AAs during Eimeria infection or vaccination programs may have a significant impact in minimizing Eimeria exposure harmful (Kim, et al.,2018).

3.1.5 Fatty acids

The high content of fatty acids and sterols in lymphoid cell membranes is a key distinguishing factor between lymphoid cells and other tissues. Supplementation with n-3 PUFAs reduces the lesion score caused by acute *E. tenella* infections (cecal or hemorrhagic coccidiosis) in broilers infected with coccidia, but not by *E. maxima* infections (intestinal or malabsorptive coccidiosis) (Allen, & Danforth,1998). Although some research found that dietary PUFA supplementation did not affect immunity or resistance to infections, there is still evidence that fatty acids can affect the immune system and release cytokines (Robinson, et al., 2018. Yang, et al., 2006). Furthermore, 0.2% butyric acid addition maintained the performance and carcass quality of *Eimeria* challenged-vaccinated broilers. Recently, a 0.750 g/kg dietary supplement with coated sodium butyrate affected the content of the cecal microbial composition (an increase in *proteobacteria* and *firmicutes* and a decrease in *bacteroidetes*) produced by *E. tenella*-infected broilers (Zhou, et al.,2017). The administration of a combination of fatty acids, acidifiers, and phytochemicals altered the duodenum structure and impacted the jejunum's inflammatory gene expression. In all dietary treatment groups of *Eimeria*-challenged-vaccinated broiler chickens, these alterations occurred concomitantly with peak fecal oocyst discharge and reduced feed efficiency (McKnight, et al.,2019). The data suggests that feeding fatty acids to coccidiosis-infected broilers may be beneficial.

3.1.6 Vitamins

Some vitamins have antioxidant, membrane-stabilizing, and immunomodulatory properties that can boost broiler resistance or tolerance to Eimeria infections (Wunderlich, et al.,2014). Deficiency in fat-soluble vitamins A (Chapman, 2014), D (Aslam, et al.,1998).and (Erf, et al.,1998). in chicken diets has been linked to lowered immunity. While fat-soluble vitamin supplements may enhance resistance to Eimeria infection, they also have some major antagonistic effects. (Kidd, 2004). Dietary supplement, β- Carotene, an important component of vitamin A, may trigger antioxidant effects, help maintain mucosal integrity, and take part in Th1 and Th2 immune responses; because of inadequate immune response and increasing oocyst shedding, its insufficiency increases vulnerability to E. acervulina infection (Chew, 1995). Changes in subpopulations of IELs in vitamin A-deficient chicks impaired mucosal immune responses during E. acervulina infection, resulting in the discharge of oocysts. (Allen, & Fetterer, 2002). Studies adjusting supplemental levels of tocopherol (the most active molecule in vitamin E) have inconsistent results, which may be impacted by variables, such as vitamin dose, bird age, and genetics (Allen, & Fetterer, 2002). A vitamin E diet containing selenium (Se), a component of glutathione peroxidase, aids in antioxidant cellular defenses, reduces cecal damage, and reduces mortality in E. tenella -infected chickens (Kidd, 2004). Dietary supplementation with DL-tocopherol acetate (vitamin E) resulted in a moderate decrease in the lesion's severity and plasma carotenoid concentrations and a minor rise in plasma nitric oxide metabolite concentrations in broilers infected with E. maxima (Allen, & Fetterer, 2002). Chickens infected with E. acervulina had low levels of ascorbic acid (Vit. C), but dietary supplementation of 1000 mg/kg reversed this effect.Broiler cellular immunity was significantly unaffected by dietary ascorbic acid supplementation (Murray, et al., 1988). Regardless of infection, diets containing commercial vitamin D-rich diets or 25-hydroxycholecalciferol (25(OH)D3 or 25D3) increased performance and mineralization, but M levels enhanced feed efficiency and mineralization much more in the existence of Eimeria infection. However, broilers infected with coccidiosis and non-infected broilers responded similarly to dietary cholecalciferol (D3) and 25-hydroxycholecalciferol (OHD) supplements at 4,000 IU/kg (Oikeh, et al.,2019).

3.1.7 Minerals

Zinc is a micro-mineral essential for growth and affects intestinal development and regeneration during and after intestinal diseases. CuZn(OH)(3)Cl (0.170 g per kg diet) mitigated *E acervulina*-induced oxidative damage in chickens. Coccidiosis hampered Zn consumption, resulting in a Zn shortage of the chick (Georgieva, et al.,2011). Because of treatment, Zn transporters and ZIP gene expression increased, and more zinc transport occurred in the jejunum than in the cecal tonsils, but more research is required to determine how the zinc source controls intracellular free zinc levels and whole-body zinc condition during treatment (He, et al.,2019). Minerals might reduce the detrimental effects of coccidiosis in broilers by modifying the host's physiology, immunology, and intestinal microbiota in health and disease scenarios. The decrease in nutrient absorption caused by *E. acervulina* depended on the content of copper and AA in the diet, although digestible changes did not impact the growth performance in *E. acervulina*-infected broilers (Bortoluzzi, et al.,2020).

3.1.8 Yeast derivatives

MOS is prebiotic, and live yeast is probiotic, but depending on the composition of the yeast cells, all other yeast supplements have different physiological effects on the animal. Yeast cells include carbohydrates, salts, monosodium glutamate, amino acids, peptides, nucleic acids, enzymes, cofactors, glucans, mannans, glycoproteins, and chitin (Shurson, 2018). Yeast cells form an interesting feed supplement because of the different components' prebiotic and probiotic properties. Yeast can be used as an entire organism or as individual components isolated from the whole yeast. Yeast-based additives include cell walls, β-glucans, and whole yeast cells. As established by MOS supplementation, these compounds have a prebiotic impact, as well as favorable effects on gastrointestinal tissue, immunological response, liver function, and growth performance (Sauer, et al., 2011; Shurson, 2018). After *Eimeria* infection, giving whole yeast cell product reduces the number of fecal and intestinal oocysts, elevates the number of cecal *Lactobacillus*, controls the expression of IL-10 mRNA in the cecal tonsils, and diminishes the number of CD8+T-cells in the cecal tonsils in pullets and layer chickens (Markazi, et al.,2017). The *Eimeria* infection slowed growth and had a detrimental impact on intestinal function and health markers. When given to BB(Ross 708 ♀ and Ross ♂) and broiler chicks, yeast bioactives enhanced IgA deposition in hatching eggs and improved jejunal villus height independent of *Eimeria* challenge(Lu, et al.,2019). The performance of birds challenged with *E. acervulina*, *E. maxima*, and *E. tenella* and treated with β-glucan was unaffected. The severity of the lesion and the gene expression of inducible nitric oxide were inducible nitric oxide synthase in the jejunum were reduced, although ileum expression was elevated. Birds also had lower levels of mucin-1 and- 2, interferon-γ, and interleukin-3. In contrast, Lu *et al*. did not find any differences in growth performance when commercial yeast or raw yeast extract were added. The addition of a yeast-derived β-glucan (Auxoferm YGT) to chicken diets altered their immune response to the *Eimeria* challenge (Omara, et al.,2021).

3.1.9 Phytogenics feed additives (phytobiotics or botanicals)

Phytogenic feed additives (phytobiotics or botanicals) are derived from specific plant components, such as roots, stems, leaves, and flowers, and include a mixture of essential oils, saponins, tannins, pungent chemicals, bitter substances, and flavonoids (Bozkurt, et al., 2014 ; Abdelli, et al., 2021). Feed International conducted global nutrition and feed studies to determine how poultry producers build antibiotic-free chick housing schemes. Thirty-five percent of respondents say they use phytochemicals and essential oils as an antibiotic growth promoters to feed formulations. Phytogenic compounds are non-antibiotic plant feed additives added as solids, extracts, or essential oils in feed (Yitbarek, 2015). The efficiency of plant components is determined by the parts of the plant used, such as shoots, bark, seeds, roots, flowers, as well as the geographical origin and harvest time of the source plant (Yitbarek, 2015; Latek, et al., 2022). Other factors that may affect the overall biological activity of plant-derived compounds include extraction procedures, housing conditions, and synergistic effects when mixing compounds (Yang, et al., 2015). Because of the wide range of compounds available, botanicals have a wide range of effects on animal physiology, including increased intestinal secretions, improved circulation, antibacterial activity, food preference, and oxidative stability of meat (Doughari, 2012). The use of plants high in plant compounds has been studied as an alternative to anticoccidial medications to treat chicken coccidiosis. While the impacts of herbal extracts from 15 different plants varied to mitigate the effects on oocyst production, survival, bloody diarrhea, intestinal lesions, and weight gain in birds infected with E. tenella, five out of 15 plants appeared to be the most effective. In E. acervulina and E. maxima challenged-chickens supplemented with oregano oil resulted in the same level of performance and damage as unchallenged birds or birds treated with salinomycin (Youn, & Noh, 2001). Phytogenics are often used in combination to target multiple parts of an animal's physiology, which can produce synergistic effects (Youn, & Noh, 2001). In Eimeria-infected chickens treated with an extract of U. macrocarpa, survival and lesion scores improved. Results on bloody diarrhea, survival, lesion scores, weight gain, and oocyst secretions showed Sophora flavescens extract was the most beneficial. (Youn, & Noh, 2001). Saponins are plant-derived phytochemicals that are effective in the treatment of chicken coccidiosis. Invasion of Eimeria sporozoite into Madin-Darby Bovine Kidney cells is reduced in the presence of thymol, carvacrol, and saponins, showing anticoccidial potential for these substances. A quillaja and yucca (saponin) combination (QY) product can cause changes in oocyst per gram of feces after immunization, but QY-fed coccidia vaccinated broilers gain immunity comparable to controls and show substantial performance and mortality benefits (Apajalahti, & Vienola2016).

4. *Eimeria* infection and gut microbiota

The ileum and cecum are two of the most important digestive areas for studying the chicken microbiome. One of the most extensively studied topics is cecal content since it has been hypothesized that bacterial populations within the cecum may reflect the effectiveness of chicken feed (Apajalahti, & Vienola2016). Residues of nutrient digestion and absorption in the proximal small intestine can be a substrate for certain bacteria in the cecum. As a result, studying the cecal microflora may reveal intestinal health in the proximal gut region and the cecum itself. The ileum is a major site of nutrient absorption and immune system regulation in the intestine, a region of Peyer's patches, lymphatic structures that spread within the epithelium and play an important role in the host's defense against microbial infections. Thus, focusing on ileum and cecal microbiota may aid in explaining the link between the gut microbiota and the host in terms of the immunological and gastrointestinal systems (Figure 4) (Shang, et al., 2018).

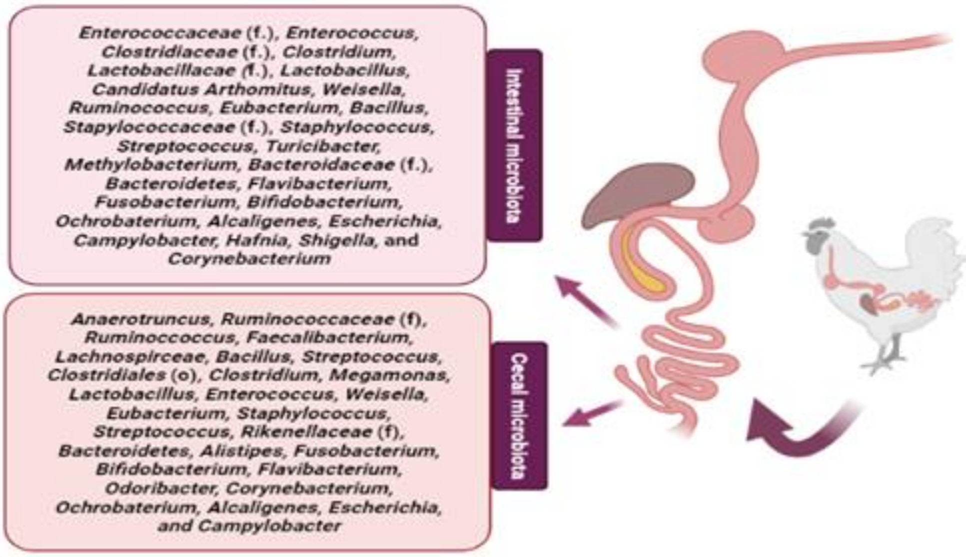

Figure 4. Chicken intestine and cecal major bacterial taxa.

Several studies have shown that geographic location influences the chicken gut microbiota. Bindari and Gerber reviewed the literature on the chick digestive microbiota and its function, the variables that impact the intestinal bacterial community and the occurrence of intestinal disease, how gut health is measured, and its relationship to performance (Bindari, & Gerber, 2022). Environmental variables, such as chicken farm biosecurity levels, feed access, chicken rearing systems, litter management, climate, and geographic region, can all impact the chicken intestinal microbiota. Rearing houses have been shown to impact non-dominant bacteria of the cecal bacterial community (Bindari, & Gerber, 2022). Because litter or chicken bedding shares many bacterial taxa with chicken fecal samples, reusing the bedding may transfer bacteria from a previous flock and alter the intestinal microbiome of a future flock(Pan, & Yu, 2014). Although the impacts of the environment on the gut microbiota have been extensively investigated, the results are still inadequately understood because several variables might influence the results both within and between studies. Because of the complex nature of these investigations, determining the specific environmental factors that may impact their outcomes is difficult (Bindari, & Gerber, 2022). Food and dietary supplements can shift the chicken gut flora or alter. The pathogenic bacterial abundance that is influenced by feed composition, as well as feed nutrient composition, has been demonstrated. Certain feed ingredients also favored several bacteria, such as higher abundances of *Lactobacillus crispatus* in sorghum-fed chickens and *Clostridium leptum* in wheat-fed chicks (Lourenco, et al., 2019). In addition, differences in nutritional value between broiler-type and layer-type diets can affect the chicken intestinal microbiota and substantially alter the immune-related gene expression after infection with *Campylobacter jejuni*. This study found that the nutritional value of food and the content of feed both influence the intestinal microbiota. Phytochemicals, exogenous enzymes, probiotics, and prebiotics influence the microbial population of the gut, including maintaining normal flora, promoting the growth of certain bacteria, and controlling pathogens (Borda-Molina, et al., 2018). In one study, L-theanine (an amino acid found in green tea extract) boosted the *Lactobacillus* population in the chicken gut and influenced the mRNA expression of many cytokine genes. Enrichment of *Lactobacilli* spp. has also been observed in the cecum of chicks given xylo-oligosaccharide prebiotics (Saeed, et al., 2019). These findings suggest that diet or supplementation affects gut bacterial communities in chickens directly or indirectly. A better knowledge of the relationship between nutrition and gut microbiota might aid poultry producers in regulating the development and health of their chickens. Interestingly, the importance of diet in controlling the gut microbiome will be better understood as the spatial and functional connections between the different parts of the avian gut and their regional bacteria are better understood (Kogut, 2022). Many gastrointestinal infectious diseases have a substantial influence on the intestinal microbiota (Macdonald, et al., 2017). According to another study, birds infected with *C. jejuni* had a greater *Clostridium* abundance than control birds. Compared with uninfected poultry, poultry infected with enteritis showed a higher prevalence of *Lactobacillus ultunensis* in the cecum (Videnska, et al., 2013). *Eimeria*-infected chickens had a surge in the number of bacteria belonging to the genera *Escherichia/ Shigella* and other *Enterobacteriaceae* family taxa (Macdonald, et al., 2017; Videnska, et al., 2013). *Eimeria* infection in chickens results in an imbalance of microbial communities and alters their activities within a host. In reaction to an infection with *E. tenella*, non-pathogenic bacteria, such as *Lactobacillus* and *Faecalibacterium* decreased, while pathogenic bacteria, such as *Clostridium Lysinobacter*, and *Escherichia coli* increased (Huang, et al., 2018). The luminal microbiota has recently been found to be more sensitive to infection-induced long-term disruption. Meanwhile, the mucosal microbiota appears to be temporarily affected, highlighting the importance of studying both the luminal and mucosal microbiota of the cecum. Recently, *E. tenella* infection affected the diversity and composition of the cecal microbiota. *Proteobacteria*, *Enterococcus*, *Incertae*, and *Escherichia-Shigella* populations decreased, while *Bacteroidales* and *Rikenella* significantly increased in the infected group compared to the control group (Zhou, et al., 2020). In birds, *E. tenella* infection disrupts the luminal and mucosal microbiota equilibrium. Recently, it has been found that the luminal microbiota is more vulnerable to long-term disruption caused by infection. Meanwhile, the mucosal microbiota appears to be only temporarily impacted, emphasizing the importance of studying the cecum's luminal and mucosal microbiota (Campos, et al., 2022). However, the replication of *E. tenella* is altered without the gut microbiota. Therefore, modulation of the microbiota and its metabolites may be an alternative approach to limiting coccidiosis's deleterious effects in poultry (Gaboriaud, et al., 2021). A metagenomics study found *Proteobacteria* (5%), *Firmicutes* (90%), *Actinobacteria* (2%), and *Bacteroidetes* (2%) in a 21-day-old chick cecal community. Bacitracin (BACI) affected proteobacteria in the vaccinated group (P = 0.03). Vaccination and nutritional interventions affected the populations of the most abundant families in the study, *Lactobacillaceae*, *Enterobacteriaceae*, *Clostridiaceae*, and *Streptococcaceae* (Das, et al., 2021). *Clostridiales* were considerably enriched at the cost of *Lactobacillales* in infected birds four days after infection with *Eimeria* spp. compared to uninfected birds. Green tea administration; however, inhibited *Clostridiales* growth and raised the relative abundance of *Melainabacteria* (Hamilton, et al., 2020). Lippia origanoides Kunth with a high thymol content improved body weight and feed conversion ratio in broilers exposed to coccidia (Betancourt, et al., 2019). Lauric acid supplementation did not diminish NE incidence or severity, although it reduced the *Escherichia/ Shigella* relative abundance. Microbiota connected with NE is a large overgrowth of *C. perfringens* and other *Clostridium* species in *Clostridium sensu stricto* 1, with a decrease in *Lactobacillus* in the jejunum. Controlling *Clostridium sensu stricto* 1 growth and manipulating *Lactobacillus* in the jejunum should be the prevention approach for NE. However, oral Akkermansia muciniphila (AM) increased NE establishment in broilers and altered the jejunal microbiota in favor of *C. perfringens* (CP) expansion. AM can be a useful probiotic in broilers, but it can be a predisposing factor for NE and should be used with caution (Yang, et al., 2022). Infection with *E. maxima* resulted in the greatest diversity of microbes in the chicken intestine. Butyric acid glycerol esters in the diet had only a small impact on the gut microbiota. These results suggest that pathogens' colonization of the chicken gut or changes in the host's defense system could cause a shift in the microbial community in the gut. Supplementing natural alternatives, such as probiotics and phytochemicals, is now the most convenient way to combat coccidiosis without risking drug resistance that jeopardizes biosecurity. Advocacy for the use of natural alternatives (feed additives) for rapid regeneration of the gastrointestinal tract and modification of the gut microbiota in response to the challenges of coccidiosis while increasing broiler growth performance and overall health (Madlala, et al., 2021). Supplementation of medium-chain fatty acids (MCFAs) to the diet reduced NE-related intestinal damage in vaccinated animals compared with other treatment groups. In addition, the same additives improve the feed conversion ratio (van Eerden, et al., 2022).

Conclusion:

The stdey addressed the following topics: economic importance, coccidiosis in poultry production, other alternative measures, and gut microbiota. More research on the association between Eimeria spp., a healthy intestinal microbial community, and intestinal immunity in natural alternatives will enable us to develop better coccidiosis control and prevention strategies in the future. Because of the problems with current coccidiosis control and the big money losses caused by infected chickens gaining too much weight and eating less food, it is important to find natural products that can help keep coccidiosis at bay and improve poultry performance so that they can be used in the live coccidiosis vaccine.

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