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Use of Tannin-Containing Plants as Antimicrobials Influencing the Animal Health

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ABSTRACT

The antimicrobial effects of diverse tannin-containing plants, particularly condensed tannins (CTs) produced from various plants, are the subject of this study. CT components can be determined using CT-specific procedures such the HCl-Butanol Acetone assay, Thiolysis reaction, and HPLC/MS analysis. These methods indicate CT contents, including mean degree of polymerization, the procyanidins and prodelphinidins ratio (PC/PD%), the isomers of trans- and cis-, and CT concentration. Tannin-containing plants possess antibacterial action, which can be attributed to their protein linkage technique, and tannin-type variations, particularly CTs extract and their PC/PD%. The effects of CT components on the development of Gram-positive and Gram-negative bacteria have been documented for their relative PC/PD%; this is regarded to be a key predictor of tannin characteristics in terms of antimicrobials. In conclusion, tannins, more specific CT compositions, have significant impacts on *in vivo* trials of animal productions and utilization of metabolites and fermentation *in vitro* experiments. More research is needed to completely comprehend how CT types affect animal feeding in terms of improved nutritional quality of animal diets, which could have consequences for human and animal health.

Keywords: tannin extracts, antimicrobials, animal health, animal feeding

INTRODUCTION

Antibacterial drugs used as performances in animals' diets were banned in Europe due to the advent of antibiotic resistance. Antibiotics in animal feed have also been shown to influence gut microbiome, raising the necessity for efficient antimicrobials to reduce damaging microorganisms and enhance animal health and welfare. Antimicrobial resistance (AMR) began to significantly impair our capacity to cure several invasive infections in the previous years, according to various publications (1). As a result, herbal medicines and plants are being studied as a possible alternative for improving animal performance while avoiding the development of antibiotic resistance. Most herbal compounds have antibacterial properties and get used as additives in animal diets rather than manufactured medications. For instance, tannins are formed as component of the secondary metabolism of various plant species, and a kind of those compounds (2).

The influence of tannin elements on bacterial growth have indeed been recorded for their comparable compositions, which is thought to be a crucial predictive of tannin antibacterial properties. Consequently, tannins have a huge effect on animal nutrition *in vivo*, as well as metabolite consumption and fermentation *in vitro* tests. Further research is needed to completely comprehend that CT-types influence animals' feeds in terms of improved nutrient value of feed additives that might have consequences for animal wellbeing (1).

Pathogenic Risks on the Diet of Humans and Animals

Annually, humans are diagnosed with a variety of pathogens that come from animals, namely *Campylobacter*, *Salmonella*, *Escherichia coli*, *Listeria*, *Staphylococcus*, and *Clostridium perfringens*, all of which may withstand some food processing. Moreover, the typical examples of these pathogens include infection of the gut that causes a direct pathological outcome, especially *Campylobacter* spp., *Salmonella* spp, *Escherichia. coli*, *Listeria* spp., from eating undercooked or contaminated animal products, whereas others are toxins caused by direct consumption of contaminated food including poorly and reheated cooked foods in which the toxins survive (1).

Campylobacter spp., for example, can induce campylobacteriosis in humans, which shows special signs including fever, acute diarrhoea, vomiting, and abdominal ache. A study has been proposed using medicinal plants or herbs that function as prebiotics to minimize faecal contamination, the amount of these bacteria in animal intestines can be decreased (3). Humans who consume contaminated chicken meat may become infected with *Salmonella* spp. and *Shigella* spp (4).

To reduce and track the microorganisms in diets, many stages could be applied during feed productions, starting on the farm with herd maintenance, which keeps away from pathogenic contamination and minimizes colonization in poultry (5, 6). Approaches to establishing a link between the plants eaten by animals and the bacteria that infect them, including the fact of certain plants containing acids can work against these bacteria, have been made (7). Heres et al. (8) have found in an *in vitro* study that sterilized standard broiler diets either acidified by organic acids at elevated level (lactic acid 5.7% and acetic acid 0.7%) or fermented by *Lactobacillus plantarum* reduced rapidly the growth of *Campylobacter jejuni* (mixture of 10 *Campylobacter* ribotypes farm isolates) and *Salmonella enterica* serovar Enteritidis phage type 4 (poultry meat isolates and resistant to nalidixic acid). Where the authors reported that there was a complete reduction within 20 min and 2 h of *Campylobacter* and *Salmonella*, respectively.

Clostridium spp. is another microorganism that induces problems in humans and animals. However, these spore-forming and anaerobic bacteria can be found in the atmosphere and inside animals (9) with human infections digesting infected birds (10), although other infection sources such as water, vegetables, and fruits may be contaminated (11). Other microorganisms, such as protozoa, may cause a disorder in the bird caecum in addition to *Campylobacter* spp., *Salmonella* spp., and *Clostridium* spp (12). Moreover, *Clostridium perfringens* could induce necrotic enteritis in poultry's gastrointestinal system, causing changes in microbiota plus the caecum environment, however, with no other predisposed factors including nutrition, management, or environmental conditions; this bacterium rarely causes necrotic enteritis in birds. As a result, proper hygiene and food management will help to minimize the number of infections (13). Animals were historically handled with specific knowledge or ethnomedical treatment that encompasses approaches for caring for, treating, and handling animals before the advent of modern drugs (14). So many Chinese scientists have investigated a variety of ordinary plant materials as potential alternative remedies, reporting benefits such as improved immune response, antimicrobial and anticancer activity, and reduced stress (15-18).

Antibiotics have been used therapeutically to manage disease outbreaks and prophylactically in animal feed at sub-therapeutic concentrations to control the burden of pathogenic bacteria in recent years. This, incidentally, provided production benefits, but it also resulted in an increase in antibiotic bacterial resistance, leading to legislate new restrictions on the use of antibiotics to promote animal production, which has been implemented throughout the food animal production industry, especially in Europe and elsewhere (19).

The use of herbal medicines and/or their extracts in various applications to develop farm-animals productivity by applying these extracts as feed supplements have been researched. Essential oils, for example, have been studied as prebiotics and probiotics in feed supplements (20). Garlic and its various bioactive components, such as polysaccharides, polyphenols, saponins, and organosulfur compounds, have been extensively reported as having medical benefits and have been utilized in the prevention and control of certain diseases (21) and could also be utilized to prevent respiratory infections in animals, such as avian influenza (22).

Jorgensen et al. (23) analyzed 241 chickens purchased from retail outlets in the UK and reported that chicken products were infected with *Campylobacter* spp and *Salmonella* spp by 80% and 25%, respectively, with *Campylobacter jejuni* accounted 98% of the *Campylobacter* spp. According to studies (25, 26), the frequency of these bacteria in bird caecum could range from 6% to 50%, with *Campylobacter jejuni* being the most common bacteria rather than other *Campylobacter* spp (24). To combat these bacteria, the host's ability to defend itself is essential.

Plants and Their Extracts to Promote Animal Welfare

As previously described, several plant materials have globally been utilized as alternative remedies for animal feeding (3). As a result, herbal medicines and plant phytochemical compositions have been used as feed additives to take advantage of their antimicrobial and biological properties (26). Many pathogenic microorganisms within the gut can be reduced or inhibited by these plants, resulting in improved animal performance (27). When researchers looked at the effects of either water plantain (*Alisma canaliculatum*) or mistletoe (*Viscum album*) as feed additives, they found that they acted as growth promoters in broilers and antibiotics (28).

Furthermore, *Sanguinaria canadensis* is used to help birds grow faster by preventing the growth of bacteria that cause digestive distress (29). Also, (30) offered broilers different doses of *Portulaca oleracea* extracts and found that these plants influenced caecal microflora by growing *Lactobacillus* and decreasing *E. coli*. In addition, *Portulaca oleracea* has been shown to benefit the intestinal ecosystem in chickens by inhibiting the growth of *Salmonella* spp and *E. coli*, thus encouraging the growth of *Lactobacillus* spp. and *Bifidobacterium* spp.

The efficacy of herbal medicine, on the other hand, will vary depending on the technique of application, the dose of active components (31) and the composition of the 'bioactive compounds.' Plant mixtures can also have the highest impact on animal performance and may improve the bioactivity of those compositions, according to research (27). The details described show how herbal plants can be used to improve animal health and treat animals that are infected. Flavanols, especially tannins, a subgroup of polyphenols, were one of the many antioxidants that can be used as food supplements or additives (32).

Tannins, on the other hand, have been regarded as antinutritional compounds, with inclusion in animal diets, potentially affecting animal output. The interactions between tannins and certain protein molecules may be to blame for these effects. Furthermore, these factors can reduce feed consumption, digestibility, and protein availability in animal diets, but these interactions are still poorly understood (33). The diverse effects of some phenolic plants in ruminants are dependent on rumen microbial metabolism, and manipulating these species is likely to improve animal efficiency (34).

Overview of Tannin Compositions

Tannins are polyphenols produced by secondary metabolites. They are divided into two categories: hydrolysable tannins (35) and condensed tannins (CT), also known as proanthocyanidins (36). CT's chemical structure is made up of flavan-3-ol subunits connected by C-4 to C-8 or C-6 to C-8 bonds (37), as shown in Figure 1.

Tannins may react with proteins, carbohydrates, lipids, and other molecules, affecting the intestinal microbiota's nutrient climate (39). Any of these compounds can also influence bacteria in the gastrointestinal tract (40). In monogastric animals, such as pigs, a variety of tannin-containing plants, particularly chestnut tannin extracts, have indeed been investigated to suppress the pathogenic impact of different *Salmonella* spp. as well as *in vitro* and *in vivo* studies of *E. coli* (41-43). By enhancing resistance to intestinal parasites, feeding tannin-containing plants to ruminants will promote weight gain, increase productivity, and fertility (44). These tannins, particularly condensed tannins, can also be fed to livestock, such as sheep and goats (45). As a result, tannin-containing plants may also serve as "nutraceuticals" meaning that they have standardised nutrients while also having medicinal properties. A recent study found that good host nutrition could help to prevent gastrointestinal infections by feeding tannins as part of a merged approach (46, 47).

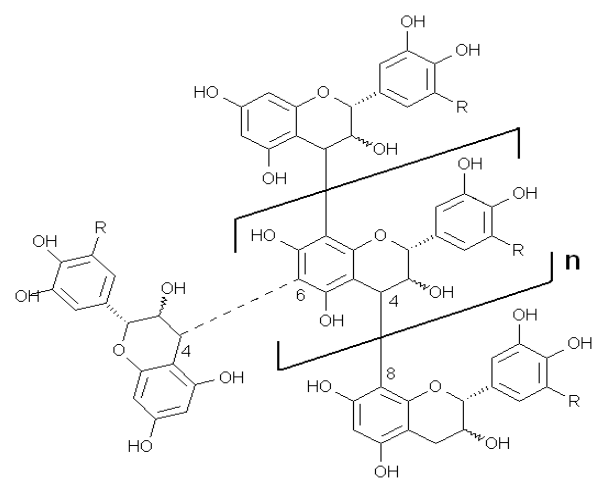

Figure 1. The chemical characteristics of condensed tannins; **n** indicates a monomeric unit; **R** indicates either H = procyanidins (PC) or OH = prodelphinidins (PD) as described by (38)

Chemical Proprieties of Tannins

Tannins, in general, are water-soluble polyphenolic compounds with molecular weights ranging from 500 to > 20,000 Da that can attach and precipitate proteins (in particular) (36). They are found in concentrations ranging from 0.5 to >30g/100 g of dry plant weight in many plants (48). As demonstrated in Figure 2, condensed tannins, like other tannin extracts, include a range of procyanidins and prodelphinidins ranging in size from short oligomers to huge polymers with cis-trans-stereo flavan-3-ol component chemistries.

Furthermore, the quantities of extractable and non-extractable tannins vary significantly. Furthermore, some CT characteristics, such as mean degree of polymerizations (mDP) and prodelphinidin ratio (PDs), as well as those have positive associations (50). Quantifying, characterizing, and isolating CTs can be done using a variety of techniques. The acid-butanol acetone assay (ABA) is one of the most popular methods for CT quantification; despite its widespread use for CT quantification, the ABA method does not provide details on CT composition. As a result, CTs were subjected to thiolytic analysis (38) as well as HPLC/MS (37). For the different CT types, this approach is useful for studying plants or extracts. Thiolysis reveals CT composition information as mDP, PC/PD, cis/trans, and flavan-3-ol ratios (51). In the majority of situations, CTs are extracted using acetone/water solvent and subsequently filtered using Sephadex LH-20 columns (39). Researchers might use this method to boost tannin concentrations in samples before utilizing them in bioassays. The CT contents of the spectra fractions are subsequently determined by thiolysis and HPLC/MS.

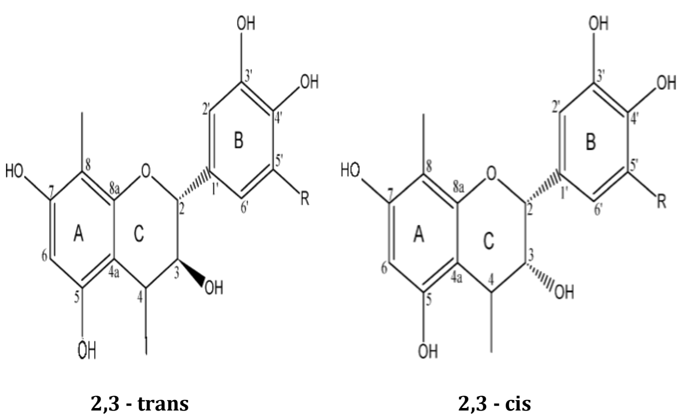

Figure 2. The structure of trans (left) and cis (right) subunits of condensed tannins; including, **R** indicates either H = procyanidins (PC) or OH = prodelphinidins (PD) as described by as described by (49)

Investigation of Tannins Using Microbial Methods

Indeed, phytochemicals contained in numerous plant materials, such as polyphenols, could be applied to reduce the pathogens in poultry (52). Several CTs were obtained, fractionated, and purified by (32) and (53) and used in microbial assays, including determining CTs' antibacterial activity concentration (MBC) that is the lowest concentration of antimicrobials, intended to control bacteria using the broth microdilution technique (54). This method allowed for a quantitative evaluation of various tannin features' antimicrobial activities *in vitro* (55). This technique is used to estimate which CT extracts are the most efficient antibacterial chemicals and what dosages should be utilized in future laboratory experiments. As previously described by (56), biofilm formation and motility tests have been utilized to study the influence of tannins on adherent bacteria (57). Using electron microscopy to examine cell damage or malformation, the impact of tannins derived from *Ocimum basilicum* L. as antibacterial agents against bacteria was investigated (58). CT extracts were tested against avian pathogenic E coli (APEC), a Gram-negative bacterial pattern, and *Staphylococcus epidermidis* (*S. epidermidis*), a Gram-positive bacteria model, by (49). CT characteristics had an important impact on these pathogens, according to the findings. The results showed that these CTs were successful against APEC and *S. epidermidis* at low doses at reduced bactericidal concentrations (MBCs). The low concentrations significantly inhibited the growth of both bacteria. Scanning Electron Microscopy (SEM) was also used in the investigation, which indicated that the plant extracts have antibacterial action against the bacterial cells (55).

CT extracts were tested against APEC, a Gram-negative bacteria model, and *S. epidermidis*, a Gram-positive bacteria model, as described by (49). CT features had an important impact on these pathogens, according to the findings. The results showed that these CTs were successful against APEC and *S. epidermidis* at low doses at reduced bactericidal concentrations (MBCs). Both bacteria's growth was significantly inhibited at low concentrations. SEM was also utilized in this study, which revealed that these extracts had antibacterial activity against bacterial cells from both Gram-positive and Gram-negative bacteria; however, CTs were more efficient against Gram-positive bacteria than Gram-negative bacteria. Surprisingly, modest doses (0.6 mg/mL) of CT extracts, which are mostly procyanidins (PC), were shown to enhance APEC development slightly in a previous study (32).

Effects of Tannins on Gut Health

Certain bioactive substances, such as short-chain fatty acids, have been shown to influence gut flora by boosting beneficial bacteria that generate butyric and lactic acid and offer an acidic pH (pH between 3.9 and 4.5) (59). During fermentation of crops, the gut microbiota produces these acids (60). A diet high in herbal remedies can help to create a favourable environment for microflora. The characterized by a high percentage of acids in fermentation feeds, on the other hand, can decrease pathogenic, foodborne microorganisms in monogastric animals (61). The mechanism of acid's effect on the entire digestive system, however, is still unknown (62). Since there is a lack of knowledge about the bioactivity of CTs in animal diets, researchers have focused on fermentation studies in the gut, as there is growing in the types of bioactive nutrients that could enhance the animal status and productivity (53, 63, 64).

Microbiota may enhance resistance to dangerous organisms in the gastrointestinal system by fermenting plant meals and then feeding nutrients to animals (65). It may also help to increase nutrient digestibility and gut morphology. Fermented feeds, on the other hand, are used as a feeding technique in monogastric animals such as pigs and chickens, rather than as an additive (60, 61). In contrast, giving pigs fermenting sugar as by-products ofcarbohydrate substitutes and a protein source resulted in a reduction in intestinal microorganisms, according to (66). This improved nutrient absorption, general health, and gut microbiome efficiency. Numerous researches looked at the link between the stomach's acid environment and the function of digestive acids in newborn pigs (67-69). A low pH can also help animals avoid pathogenic illnesses; moreover, an acidic environment has been shown to improve the intestinal microbiota of birds (70).

According to (71) who identified the benefits of fermentable sugars in mono-gastric meals, carbohydrate fermenting of short-chain fatty acids could be absorbed through bacteria. The structure and features of CT metabolism in ruminants do not alter throughout the digestive route, indicating that if CT has an antibacterial impact, it will occur together with the digestive system (72). Nonetheless, CT concentrations varied depending on the pH value of the compartment, with an acid of the abomasum, being more accessible than neutral of rumen or even in alkaline of the small intestine.

Tannin Impact on Metabolic By-products

In vitro fermentations are useful for predicting the biological activity of tannin compositions because they model events using chicken gut contents. Furthermore, a basic batch culture technique was used to perform *in vitro* fermentation in the presence of CTs for 24 h under strictly anaerobic conditions. Following that, an *in vitro* chicken caecum model was used (49). This method requires an effective medium and inoculum to simulate conditions found in the gut, including temperature and pH values (73). It is a versatile and valuable method for *in vitro* studies of caecal microbiota and metabolites (74, 75).

The nuclear magnetic resonance (NMR) technique could be used to collect data on metabolites (e.g., amino acids, carbohydrates, and fatty acids), as well as knowledge on digestion and degradation methods, using fermentation (76). NMR spectroscopy-based metabolic analysis is a high-throughput technique that involves little sample preparation (77). Powerful magnetic fields and radio-frequency signals are applied to the nuclei of atoms in NMR spectroscopy. The presence of a magnetic field causes the nucleus of these atoms with an odd atomic number (1H) to spin. The nuclei will then be promoted from low energy to high energy spin states because of the absorption of such pulses, and the resulting emission of radiation during the relaxation process will be observed (78). A recent study examined CTs using the ^{13}C NMR technique, which determined CT contents in some tannin-containing plants such as sainfoin, blackcurrant and tilia. This technique helped to CT compositions and concentrations in extractions, fractions, and milled tissues. This technique also provided a possible insight to detect the high molecular weight of CT plants and their extracts (79).

A metabolic investigation is particularly beneficial for simultaneously determining numerous bioactive compounds as well as identifying quantitative changes in these chemicals. As (80) demonstrated, NMR spectroscopy can assess metabolomics shifts and characterize the existence of mass spectrometry modulations; CTs may be tracked to see how it impacts fermentation and end-products.

A recent study investigated the effects of fermented animal feeding which is associated with gut microbiota using different methods such as metagenomics sequencing analysis and HS-SPME-GCMS. These techniques were applied in this study to characterize the fermentation end products of some aromatic plants (e.g., tannins). The study reported that microbial communities showed significant changes through the fermentation processing leading to an increase in flavonoid compositions and recorded a significant change at the microbial communities during fermentation, which could suggest that microbial succession for the assimilation of fermentation by-products leading to the production of flavonoids (81). Currently, a rapid development happened every day to determine and investigate the effects of fermented products on the microbial population in the gut. Recently, sequencing technology and bioinformatics were applied to identify the complexity of microorganisms in the gut that could generate by fermented food processing. This kind of study may provide baseline data for the product industry (82).

In general, this review focused on one group of polyphenols, which is called 'tannins' and more specific are CTs. Different methods were used to assess their actions, including measuring different CT doses and compounds against pathogens that can harm animals. Using various CT compositions and concentrations indicated that high tannin contents were more effective than low doses at reducing bacterial activities. Furthermore, these compositions demonstrated significant impacts on bacterial MBCs. Tannins and their extracts can affect positively bacterial strains but with different concentrations. In *in vitro* fermentation, their compositions had an important impact on the synthesis and utilization of metabolites. More research is needed to determine how other CT types affect animal diets in terms of improved nutritive value, which could affect human health.

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CONFLICT OF INTEREST

There is no conflict of interest declared by the authors.

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