Review of literature

Economic losses in the poultry industry are mainly due to various diseases. According to Jordan and Pattison (1996) and Calneck et al. (1997) poultry diseases can be divided into five groups namely bacterial, viral, fungal, parasitic and non-infectious diseases affecting chicks and growers. Furthermore, studies have shown that other diseases are present in scavenging poultry communities (Bell, 1992; Cumming, 1992; Chrysostome et al. 1995 and Kusina et al. (1999) pointed out through a survey on village chicken losses in Zimbabwe that aside from the predators and New Castle disease, coccidiosis, directly or indirectly, represents an important cause of chick mortality during the first three weeks of age. Other causes of poultry losses are lack of supplementary feed, sub-optimal management (Pandey, 1992; Bagust, 1994) and a variety of predators.

Coccidiosis

Coccidiosis remains one of the most expensive and common diseases of poultry. Infection cause decreased growth rate and if severe, mortality (Poonsuk, 1993).

Causative organism

In most cases, broiler flocks are infected with five or more species of Eimeria (Muangyai et al, 1990). Recently, Eimeria tenella has become the most pathogenic and important species, followed by Eimeria necatrix (Muangyai et al., 1987). Soulsby (1968) collected data on the species that have been reported in the domestic chicken:

Eimeria acervulina Tyzzer, 1929
Eimeria brunetti Levine, 1942
Eimeria hagani Levine, 1938
Eimena maxima Tyzzer, 1929
Eimena mivati Edgar and Siebold, 1964
Eimena necatrix Johnson, 1930
Eimena praecox Johnson, 1930
Eimeria tenella (Railliet and Lucet, 1891; Fantham, 1909)

Transmission

Coccidiosis should be regarded as ubiquitous in poultry management, since even under the extreme conditions of experimental work, it is difficult to avoid infection completely for any length of time. Essentially, the clinical disease entity depends on the number of oocysts ingested by individual birds (Fernando, 1982). After ingestion of the oocysts, the outer cover is broken down in the stomach of the birds and the free sporozoite move to the intestinal wall where they multiply. New oocysts are formed which leave the animal with the faeces. The life cycle of Eimeria spp in chicken is presented in Figure 1. Oocysts persist in litter. If the environmental hygiene is poor, the number may be very large and this is particularly so with E. tenella which has a high biotic potential. Where young birds are placed on heavily contaminated litter, death may occur within a few days and up to hundred percent may die.

The environment is being contaminated continuously, even from immune birds, though the initiation of an outbreak depends upon factors which allow oocysts to sporulate and remain viable (Muangyai et al. 1990). For sporulation oocysts require moisture and warmth and they survive best in shaded, moist conditions. Poorly maintained litter houses may well supply such needs and excessive numbers of sporulated oocysts may be found in poorly kept quarters (Soulsby, 1968).
Parasites continue to multiply

Parasites enter intestinal cells of bird and multiply

Oocyst is ingested by another bird

Male and fer parasites ir new oocysts

Infected birds spread "oocysts" or protective capsule containing parasites

Oocysts "sporulate" or become infective in moist litter

Figure 1: Life cycle of Eimeria sp.
Principle symptoms

Coccidia are found in all chicken from four to ten weeks of age. Depending on the amount of oocysts intake, primary signs might not be obvious. Lightly infected birds might not look ill but the feed intake will be lowered, feed efficiency is less and the birds loose weight. Layers will have lower egg production. By severe infection the birds sit, look ill, get hemorrhagic diarrhea and might die after twelve to fifteen days.

Lesions

Diagnosis of coccidiosis in chicken is best done by post mortem examination of birds (Poonsuk, 1993). Diagnosis on faecal examination may lead to quite erroneous results. For example, the major pathology is produced before oocysts are shed in the faeces (e.g. *E. tenella*) and the presence of large number of oocysts may not necessarily indicate a serious pathogenic condition. With *E. acervulina*, which has a high biotic potential, comparatively larger number of oocysts are shed per oocyst given than with *E. necatrix* (Suksaithaishana, 1989). Moreover, the accurate identification of the oocysts of various poultry coccidia is not easy. Mistakes can be avoided by post mortem examination (Soulsby, 1968). The location of the major lesions gives a good indication of the species of coccidia concerned. For example the haemorrhagic lesions in the caecum would suggest *E. tenella* (Muangyai et al, 1990).

Lesion scoring, where the lesions in intestinal tract of poultry are determined, is one way of diagnosing the severity of this disease. The lesion and infection of the organ are given scores from 1 - 4, 1 for no lesion found, and 4 for severe lesions (Johnson and Reid, 1970).

Treatment

As treatment sulfadimethazine 2 g/l drinking water or sulfaquinoxaline 0.25 g/l drinking water for 3 days twice at 2 days interval is suggested (Say, 1995).
Prophylaxis

In broilers, turkeys and layer coccidiostats replacements such as amprolium: 0.012% in mash feed up to twelve weeks prevent clinical disease. Anticoccidial drug susceptibility tests has shown that sulfa dimethoxine are more effective compared to others coccidiostats as preventive medication (Frazier, 1987). Tanawongnuvet and Muangyai (1990) found that trimethoprim mix with sulfaquinoxaline sodium with 1:5 in 500 ppm for four to five days was very effective for coccidiosis infections with *E. tenella*. However, some isolated coccidia species showed complete or partial resistance to some kinds of drugs. Due to problems of drug resistance, shuttle and rotation programmes are used.

Use of antibiotics in animal production

Antibiotics are used frequently in modern agriculture practice: both to prevent disease, and in higher dosage forms, for the treatment of individual animals for specific disease conditions. Apart from this, antibiotics are also used on a herd basis as additives to feed and water to promote weight gain and improve feed conversion efficiency. Such usage may lead to problems with residues in agricultural products and to environmental contamination.

Antibiotic residues in animal meat

The residues of antibiotics in animal meat can enter human food and increase the risk of ill health in persons who consume products from treated animals. To solve this problem, the inspection of agricultural products for unacceptable residues is one of the most important duties of public health. The thirty sixth Joint meeting of Food and Agriculture Organization (FAO) and World Health organization (WHO) expert committee on food additives meeting in 1990 established "maximum residue limit" (MRL) for oxytetracycline of 600 microgram/kg in kidney; 300 in liver; 100 in muscle; 100 in milk; 200 in egg and 100 in fat for all species for which residue depletion data were provided (cattle, swine, sheep, chicken, turkey and fish) (JECFA, 1990). The fortyfifth Joint FAO/WHO expert committee on food additives meeting in 1995 allocated the
same MRL, except for milk where also MRL for chlortetracycline and tetracycline additional to those previously allocated to oxytetracycline at the thirtysixth meeting where established: 100 microgram/kg for muscle (cattle, pig, poultry), 300 for liver (cattle, pig, sheep, poultry), 600 for kidney (cattle, pig, sheep, poultry) and 200 for eggs (poultry) (JECFA, 1995). Still residues are found in animal products. Al-Ghamdi et al. (2000) found residues of tetracycline compounds in poultry products in the eastern province of Saudi Arabia. They collected chicken muscle, liver and egg samples from thirtythree broiler and five layer farms over a period of two years. Antibiotic residue positive samples were identified in the products of 23 (69.7%) broiler and 3 (60%) layer farms. Also Williama (1999) reported, that shipments of pork from the United States to other countries have been rejected because of the alleged presence of residues of tetracycline. Bunyapraphatsara (2000) reported that in Thailand the excessive use of antibiotics including virginia cin, spiramycin, bacitracin and avopacin leads to residue contamination of the meat products. This has led to the ban of meat by EU and Japan.

 Problems of antibiotic resistant microorganisms in animal production

Some bacteria become resistant to antibiotics (Hisao et al. 1995). Lopes et al. (1979) found that broiler chicks which had received tetracycline and chloramphenicol in drinking water had antibiotic resistant E. coli in the intestine. Ohya and Sato (1983) found also that feeding of diets containing antibiotics to broiler chicken may possibly affect the stability of the intestinal microflora. Molitoris et al. (1986) described that Streptococcaceae in faeces of broilers which were fed diets with chlortetracycline were resistant to antibiotics. Chaisrisongkram (1992) reported that on some duck farms in Thailand there were problems of resistance against antibiotic drugs for against fowl cholera. Hisao et al. (1995) reported that antibiotics and antimicrobial compounds in food have effect on the human gut flora and the residues of them may give rise to resistant pathogens in the human gastrointestinal tract or that adventitious organisms may gain a hold.
Control of coccidiosis in chickens

Management

Because coccidial oocysts are ubiquitous and easily disseminated in the poultry house environment and have such a large reproduction potential, it is very difficult to keep chickens coccidia free, especially under current intensive rearing conditions. Oocysts sporulate readily in poultry house litter. However, bacteria, other organisms, and ammonia that are also present can damage them, and their viability can begin to diminish after three weeks (Williams, 1995). Many producers basically remove caked litter, let the houses air out for two to three weeks, and top dress with fresh litter before placing a new flock. On the other hand, it is common practice of many other producers to do a thorough cleanout between flocks. This practice may become more widespread as the effectiveness of anticoccidial continues to decrease and the use of live vaccines increases. Biocontrol measures such as requiring caretakers to change clothes between houses can minimize the spread of infective oocysts. The practice of strict biosecurity is essential in the care of broiler breeders.

Immunobiology

Day-old chicks do not normally derive passively transferred protective immunity from the hen and birds of any age are susceptible to coccidiosis. In practice, most acquire infection in the first weeks of life and this infection induces a good immunity. In most situations this persists for life (Alexander, 1991), due to frequent low-grade re-exposure to infection but, in the absence of infection, immunity may wane. A cardinal feature is that immunity is species specific. Thus, in chickens for example, immunity to *Eimeria tenella* does not confer resistance to *Eimeria maxima* etc (McDougald, 2003). Within species there appears to be remarkably little strain variation and strains of the same species isolated from widely separated locations will provide substantial cross-protection. However, important exceptions are *E. maxima* and *E. acervulina*. Immunity is best engendered by repeated exposure to low number of oocysts, so-called trickle
infection Immunity is manifested as a reduction in lesions and a marked reduction in oocyst output due to both a reduction in the number of sporozoites that successfully invade host cells and inhibition of intracellular development of those that do (McDougald, 1997). The effectors of immune response to primary and challenge coccidial infections are primary T cells residing in the gut associated lymphoid tissues. Humoral immune responses also occur, but antibodies play a minor role in resistance and immunity to coccidian (Chapman 1999a). According to McDougald et al. (1997) vaccines must contain all the important species because of the species specificity of immunity.

Drugs and their mode of action

Each class of chemical compound is unique in the type of action exerted on the parasite, and even in the developmental stage of the parasite, most affected. The chemical mode of action of some drugs is known to be highly detailed event, and the action of other drugs remains a mystery (McDougald, 2003). The sulfonamides and related drugs compete for the incorporation of folic acid. Amprolium competes for absorption of thiamine by the parasite. The quinoline coccidiostats and clopidol inhibit energy metabolism in the cytochrome system of the coccidia. The polyether ionophorous upset the osmotic balance of the protozoan cell by altering the permeability of cell membrane for alkaline metal cations (Jeffers et al. 1997). The coccidia are prone to attack by drugs at various stages in the development in the host. Totally unrelated drugs may attack the same stage of parasite. The quinolones and ionophorous arrest or kill the sporozoite or early trophozoite. Nicarbazin, robenidine and zoalene destroy the first- or second-generation schizont, and the sulfonamides act on the developing schizont and on the sexual stages. Diclazuril acts in early schizogony with *E. tenella* but is delayed to later schizogony with *E. acervulina* and to the maturing macrogamete with *E. maxima* (Chapman, 1999). The time of action in the life cycle has been construed as having significance in the use of drugs in certain types of programmes in which immunity is desired, but there is no good evidence that this is true under practical conditions.
Drug resistant

It is quite clear, however, (Chapman, 1994 and 1999; Ruff et al. 1966), that some degree of resistance to all anticoccidial drugs, including ionophores, has developed. To minimize the effects of resistance, poultry producers rotate the use of various anticoccidials with successive flocks, combine chemical and ionophore treatments, or employ shuttle programmes during a flock grow out.

Application of these treatment programmes depends on seasonal conditions and prevalence of various species of coccidia (Williams, 1999). In recent years, pharmaceutical companies have not brought new anticoccidials to market. Two potential drug targets, enzymes of the sporozoite mannitol cycle (Allocco et al. 1999, Schmatz, 1997) and trophozoite histone deacetylase, have been identified (Schmatz, 1997). According to Long (1982), the continuous use and misuse of anti-coccidial drugs have led to the emergence of drug-resistant strains. Furthermore, drug- or antibiotic-residue in the poultry products is potentially annoyance to consumer (Youn et al. 2001). Therefore, other alternative treatment such as medicinal plant used in coccidiosis control must be envisaged, since coccidiosis was reported to be the most important parasitic disease for village chick (Kusina et al. 1999).

**Alternative controls including feed additives and medicinal plants feed additives**

Many different types of substances have been investigated in the search for alternative controls of coccidiosis. A number of natural products or feedstuffs have been tested as anticoccidial dietary additives. Some of this work has been reviewed (Allen et al. 1998). Sources of fats containing high concentrations of n-3 fatty acids (n-3 FA) (docosahexaenoic acid, eicosapentaenoic acid, and linolenic acid), such as fish oils, flaxseed oil, and whole flaxseed, when added to starter rations and fed to chicks from one day of age, effectively reduced lesions resulting from challenge infections with *E. tenella* (Allen et al. 1996 and 1997) but not *E. maxima* (Allen et al. 1997). The fish oil and flaxseed oil diets significantly reduced the degree of parasitization by and development of *E. tenella* (Allen et
al. 1996) and caused ultrastructural degradation of both asexual and sexual stages, characterized by cytoplasmic vacuolization, chromatin condensation within the nucleus, and lack of parasitophorous vacuole delineation (Danforth et al 1997). These results are consistent with reports of the effects of high n-3 FA diets on other parasites (Allen et al. 1998) and suggest that these diets induce a state of oxidative stress (due to the high concentration of easily oxidized double bonds) that is detrimental to parasite development.

**Medicinal plants**

**Chemical compounds**

According to Kayser et al., (2002) the plant medicinal properties are ascribed to the following chemical compounds contained in the leaves, roots, fruits and seeds.

*The alkaloids* are common to many plants and form the basis of many modern drugs such as morphine, atropine and codeine. They contain nitrogen and are usually alkaline. The plant makes them from its amino acids or protein building blocks. They can cross the blood brain barrier and in excess can be toxic. In excess they cause liver damage. The younger leaves tend to have more alkaloids.

*The bitter* tends to stimulate the secretion of gastric juices and prime the pancreas to produce more enzymes. The result is often an improvement in resistance to gut infection and death of bacteria.

*The flavonoid* and *bioflavonoids* are antioxidant, improve the potency of vitamin C, prevent tumor formation and reduce coronary heart disease. Estrogenic flavonoids occur in legumes and linseed.

*Glycoside*, a component of the very powerful heart drug digitalis, is extracted from foxglove.

*The saponins* make the herbs more soluble. They can cause red blood cell breakdown by dissolving their membranes. They lower plasma cholesterol and may affect bowel flora.
The tannins are large phenol compounds, which bind proteins on mucous surfaces so that they become less permeable. This is called an astringent action. They are poorly absorbed and produce a protective layer of coagulated protein, which stops diarrhea, reduces gut motility and numbs nerve endings.

The oils are different in each plant. There are seven major groups. They are extracted and concentrated and called Essential oils. They can be toxic when taken internally in the concentrated form.

**Plant anti-coccidial activities**

Feed supplementation with antioxidants such as -tocopherol (8 ppm), found plentifully in seed oils such as wheat, corn, and soybean, and the spice turmeric (1%), as well as its main medicinal component, curcumin (0.05%), appear effective in reducing upper- and mid-small intestinal infections caused by *E. acervulina* and *E. maxima* (Allen et al. 1998). They are not beneficial for *E. tenella* infections, however.

Artemisinin is a Chinese herb isolated from *Artemisia annua*; it is a naturally occurring endoperoxide with antimalarial properties. It has been found effective in reducing oocyst output from both *E. acervulina* and *E. tenella* infections when fed at levels of 8.5 and 17 ppm in starter diets (Allen et al. 1997). The mode of action is also thought to involve oxidative stress.

In Thailand Naiyana, (2002) used *Andrographis paniculata* leaf powder at 0.1, 0.2, 0.3 and 0.4 incorporation level in the feed and found out a significant positive effect of the plant on mortality rate (0%, 42.85%) for 0.4 *Andrographis* feed incorporation group and control group. This is in agreement with the observation of Sujikara (2000) who also reported lower mortality rates after supplementation of the same leave powder, though clinical disease and mortality may occur in heavy coccidiosis infection, especially in broiler, layers or breeders (Poonsuk, 1993). Also the control group had the highest lesion score 3.33 compared to the treated group.

Most recently, extracts from fifteen Asian herbs were tested for anticoccidial activity against *E. tenella*. Of the species tested, extracts from
Sophora flavescens was the most effective in reducing lesion scores, maintaining body weight gain, and reducing oocyst production (Youn et al. 2001).

The polysaccharide extracts from two mushrooms, *Lentinus edodes* and *Tremella fuciformis*, and a herb, *Astragalus membranaceus*, when given as supplement feed to chickens resulted in a significant impact on the inductive responses against *E. tenella* infection in chicken by enhancing both cellular and humoral immunity (Guo et al. 2004).

Gefu et al. (2000) reported that among many plants used in the treatment of parasitic and protozoan diseases of poultry in Nigeria, *Boswellia dalzielli* has been successfully used for the treatment of coccidiosis and amoebic dysentery.

Giannenas et al. (2003) reported that the essential oil of oregano, an aromatic plant of Labiatae family exhibited coccidistatic action against *E. tenella* when incorporated into chicken diets at the level of 300 mg/kg.

Christaki (2004) investigated the effect of a dietary mixture of herbal extracts on the performance of broiler chickens experimentally infected with *Eimeria tenella*. The herbal extracts used in this study constitute the active components of Apacox (APA-CT, s.r.l., Italy), a naturally derived nutrition enhancer that contains extracts from the plants *Agrimonia eupatona*, *Echinacea angustifolia*, *Ribes nigrum* and *Cinchona succirubra*. The results indicated that Apacox exerted a coccidiostatic effect against *E. tenella*.

Murtaza (2002) compared the anticoccidial efficiency of neem fruit (*Azadirachta indica*) with an ionophorus anticoccidial, Kokcisan (Salinomycin sodium) against coccidiosis in broilers. One hundred and fifty gram of neem fruit per fifty kg feed had excellent performance in terms of oocyst count and lower mortality as compared to other treated groups.

Thus, medicinal plants if promoted to smallholder farmers can reduce significantly the impact of coccidiosis and improve the productivity (Naiyana, 2002).