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Review on Toxoplasma Metabolism and Potential Drug Targets for Chemotherapy

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Abstract: Toxoplasmosis is one of the most common parasitic diseases of animals and man. The definitive hosts for the parasite are members of the Felidae family (mainly domestic cats). *Toxoplasma gondii* is an obligate intracellular parasite that is capable of infecting a variety of intermediate hosts (all warm-blooded animals) including humans. The prevalence depends on many factors but is primarily related the availability and ingestion of infected intermediate hosts (cat's rodents, birds etc). Infection is therefore more common in stray and feral cats than in pet. Infection with *Toxoplasma gondii* in human is a major health problem, for immunocompromised individuals, such as HIV-AIDS patients, organ transplants recipients and unborn children of infected mother. *Toxoplasma gondii* and other parasites of phylum apicomplexa reside and replicate exclusively within eukaryotic cells suggests that these parasites depend on the metabolism of their hosts and that they have evolved metabolic pathways reflecting their intracellular lifestyle. The metabolism of Toxoplasma, denotes its capability of converting biochemical compounds into products in which their growth and survival of the parasites. This process occurs in a series of biochemical reactions, catalyzed by enzymes, which are organized into metabolic pathways which in turn interconnect to form a complex and intricate metabolic network, which includes energy, protein and nucleotide metabolism that are not taken place in the host cell, these used the potential targets for chemotherapeutic intervention in *T. gondii*. Current drug treatment against toxoplasmosis targets the folate biosynthesis pathway, which is absent in human metabolism. Current therapy of toxoplasma is the combination of trimethoprim and sulfamethazole; however, patients that are intolerant to pyrimethamine and sulfamethoxazole are usually intolerant to this therapy due to similar mechanism of action. But pyrimethamine and sulfadiazine is the treatments of choice for toxoplasmic encephalitis in patients with AIDS.

Key words: Chemotherapy · Metabolism · Toxoplasma.

INTRODUCTION

Toxoplasma is a worldwide zoonotic, intracellular protozoal parasite that affects humans, animals and birds. However, its incidence is high in particular area [1]. The parasite has a higher prevalence found in warm and moist area than cooler or dry area [2]. The cats and other felidae are the only definitive host of *Toxoplasma gondii*. All warm blooded animals including humans are intermediate host that harbor tissue cyst in their bodies. It is transmitted by ingestion of oocyst in contaminated food and water or under cooked meat containing tissue cyst and congenitally (mother-to-fetus) [3]. Infection with *toxoplasma gondii* in human is a major health problem, for immune compromised individuals, such as aids patients, organ transplants recipients and unborn children of infected mothers [4].

Toxoplasma and other parasites of phylum apicomplexa depends on the metabolism the host and that they have evolved metabolic pathways reflecting their intracellular lifestyle of this parasite. The metabolic pathway of the parasite has a direct implication for understanding of parasite's requirements for intracellular growth. Furthermore, these pathways provide unique targets for compounds designed to inhibit and eradicate infection caused by this important humans and animals' pathogen [3].

The unique aspect of the electron transport chain (etc) complex and their related enzymes represent promising drug targets for chemotherapy. A cytochrome independent alternative oxidase (aox) in the parasite is a leading drug target. Drug resistance highly limits the arsenal of availability drug against protozoal parasites, particularly mutations of cytochrome b-gene of etc or

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change in iron homeostasis by mitochondrial enzyme aconitase alter the sensitivity of multidrug resistance (mdr) and regulate resistance level to anti-parasitic drugs [5].

Therefore, The Objectives Of This Seminar Paper Are:

- To review the metabolism of *toxoplasma gondii*
- To review on potential drug targets and chemotherapy of *toxoplasma*

Epidemiology and Zoonotic Importance of Toxoplasma: Toxoplasmosis is a zoonotic disease, naturally affects humans, domesticated and wild animals and birds. The disease occurs throughout the world through infection rate differing significantly from country to country. The infection rate varies greatly from country to country, causing the disease to spread around the world. Some incidences of 34-59% in dogs, 34% in cats, 47% in cattle, 30% in pigs, 2% in humans and 48% in goats are reported in surveys based on serological findings conducted in the United States [1]. The parasite can infect almost any warm-blooded animal, albeit the rate of infection and susceptibility varied depending on the species. Chronic toxoplasmosis is more common in sheep and goats among livestock pigs [6].

There are significant differences in the prevalence of *toxoplasma gondii* in meat-producing animals within and between countries. It has been demonstrated that different farming and management techniques have a significant impact on the rate of infection. For example, animals raised outdoors or in a free-range setting are more likely to contract toxoplasma gondii than those raised indoors or in commercial confinement operations [2].

The only known definitive host for toxoplasma gondii, which reproduces sexually to create infectious oocysts, is the cat and other felidae. It has been estimated that between 30 and 40 percent of domestic cats globally have t. Gondii sero-prevalence. Domestic cats' rates of toxoplasma infection vary greatly based on their diet and lifestyle. Compared to domestic cats, feral cats that forage for food are more likely to get infected. The availability of infected birds and small animals determines the incidence of t. Gondii in the cat population and frequently, this availability is high [6].

For one to two weeks, the majority of infected cats only shed oocysts once in their lifetime. Millions of oocysts can be shed during this this time, even though it is just temporary. Each oocyst has the ability to spread and endure for months. Approximately 1% of cats are thought to be actively shedding oocysts at any given moment. For immune-compromised individuals, including aids patients, organ transplant recipients and the fetuses of infected mothers, t.*gondii* infection poses a serious health risk [2, 4, 7]. Workers in slaughterhouses, farmers and veterinarians who handle contaminated items run the risk of contracting toxoplasmosis at work. Contact with an infected cat increases the risk even further [8].

Transmission can occur through a variety of pathways both within and between host species. *T. gondii* is vertically transmitted during pregnancy by tachyzoites, which are then transferred to the fetus through the placenta. Ingesting infectious oocysts from the environment or consuming tissue cysts or tachyzoites found in meat or primary offal (viscera) from a variety of animals are examples of horizontal transmission of *T. gondii*. Tachyzoites found in blood products, tissue transplants and unpasteurized milk can also spread the disease. Which of these paths is more significant from an epidemiological standpoint is unknown, though. In the past, eating raw or undercooked meat—especially from sheep and pigs—was thought to be a key way for the disease to spread to people [9]. *T. Gondii* was less common in meat-producing animals in regions with strict farm management. For instance, the frequency of t. Gondii in fattening pigs is currently less than 1% in a number of Eu countries. Given these facts, pork is probably no longer a significant cause of human infection in these countries. However, among human populations with varying cultural and dietary practices, the main routes of transmission are probably different. Recent human acute toxoplasmosis epidemics in the americas have been linked to environmental oocyst contamination [10].

Metabolism in Toxoplasma Parasites: The term metabolism refers to the chemical reactions that take place in the bodies of organisms. *Toxoplasma gondii* and other parasites of phylum apicomplexa reside and replicate exclusively within eukaryotic cells suggests that these parasites depend on the metabolism of their hosts and that they have evolved metabolic pathways reflecting their intracellular lifestyle. The chemical reactions that occur within an organism's body are referred to as metabolism. The fact that *toxoplasma gondii* and other phylum apicomplexa parasites only live and reproduce inside eukaryotic cells indicates that they are dependent on their hosts' metabolisms and have developed metabolic pathways that reflect their intracellular lifestyle. Understanding the parasite's needs for intracellular growth is directly impacted by its distinct metabolic

pathways. Additionally, these pathways offer distinct targets for substances intended to prevent and eliminate infection brought on by these significant pathogens that affect both humans and animals [11].

Toxoplasma is an intracellular parasite that is known to alter host cellular functions in order to provide the nutrients needed for parasite growth, defend against host defenses and promote replication and spread. The parasite alters the host cytoskeleton during invasion and parasitophorous vacuole formation by rearranging intermediate filaments, capturing microtubule organization centers and forming connections with the er and mitochondria. Many mitochondrial and several proteins are induced during tachyzoite infection, changing the complement of host proteins. The host cell's subversion alters transcription, prevents apoptosis and guarantees the delivery of vital nutrients (such as cholesterol, polyamines and purines). *T. Gondii* obtains its supply of different amino acids by a combination of synthesis and salvage. For instance, tryptophan and arginine are auxotrophic for the parasites [12].

Energy Metabolism: The mitochondria is typically described as the cell's power source. Acetyl coa, the last metabolic product of glucose and other foods that provide energy, is effectively converted to atp at this location via the tca cycle. Toxoplasma reproduces in the vacuoles of host cells, where it needs nutrition and host carbon (glucose) to grow that the intracellular *t. Gondii* stages actively catabolize host glucose through the mitochondrial mechanism known as the canonical, oxidative tricarboxylic acid cycle (tca cycle), which breaks down organic molecules to produce energy. Through the tca cycle and an unidentified ã-amino butric acid (gaba) shunt, these stages also catabolize glutamate, which promotes intracellular parasite proliferation [13].

Gaba may serve as a short-term energy store because parasites without the gaba shunt show reduced growth and are unable to continue motility in nutrient-limited conditions. Because of their metabolic adaptability, t. Gondii tachyzoites can probably infect a wide variety of cell types [14]. Despite having cristate mitochondria, which are normally linked to mitochondrial respiration, tachyzoites mostly rely on glycolysis to produce energy. Additionally, bradyzoites use phosphofrutokinase, a glycolic enzyme that is 2-3 times less abundant in bradyzoites than in tachyzoites [15].

Bradyzoites in toxoplasma gondii acquire a lot of amylopectin granules and a lot of michronemes. The tachyzoites, on the other hand, have fewer michronemes and no amylopectin. When the latent and encysted bradyzoites transform into the quickly replicating tachyzoites, amylopectin is most likely eaten. Since amylopectin degrades or serves as a substrate for glycolysis or mitochondrial oxidative phosphorylation, it offers an energy source [13].

Enzymes of Energy Metabolism in the Toxoplasma: *Toxoplasma gondii* and other apicomplexan parasites depend on a number of essential enzymes for the metabolism of carbohydrates in order to survive. The parasite should be able to convert crucial glucose into pyruvate since the cytosol includes a full complement of glycolysis-related enzymes. The genome of toxoplasma gondii contains all of the glycolytic enzymes, ranging from phosphofrutokinase to pyruvate kinase. The activities of phosphofrutokinase, pyruvate kinase, lactate dehydrogenase, nad (+) and nadh-linked isocitrate dehydrogenases and succinate dehydrogenase were examined in the bradyzoite and tachyzoite forms of toxoplasma gondii that were isolated from infected animals [15].

Protein Metabolism in Toxoplasma: Toxoplasma is an obligatory intracellular parasite that depends on the coordinated release of a protein from its transmembrane micronemal protein 2 (micp2), which combines host cell identification with the parasite's cytoskeleton rearrangement to promote invasion [16]. The tachyzoite-specific major toxoplasma surface protein sag i plays a direct or indirect role in the cellular processes that cause chemokine ligand 2 (ckl2) secretions following infection with t. Gondii. The surface of toxoplasma gondii tachyzoites is dominated by glycosyl phosphatidyl inositol (gpi) anchored proteins, as is the case with many other protozoan parasites [17].

It is still unclear how *T. gondii* gpi-anchored proteins are made and moved from the parasite pellicle's peculiar triple membrane structure to the plasma membrane. Toxoplasma gondii's calcium-dependent protein kinases 1 (cdpk 1) (tgcdpk) have emerged as desirable targets for the development of selective inhibitors to counteract the infection those protozoa cause. Kinase inhibitors are a significant class of treatments because protein kinases are implicated in numerous diseases and have emerged as an appealing target class for drug development. In order to phosphorylate a particular residue on their protein substrates, kinase uses atp [18].

Nucleotide Metabolism in Toxoplasma: The majority of apicomplexa have significantly adapted to their host environment and their host specificity is very limited. As common for protozoa, apicomplexans cannot synthesize purines from scratch. Pyramidine can be synthesized de novo by most, but not all. Pyrimidine can also be salvaged by some, but not all. The purine salvage mechanism in the apicomplexa is the same because of this shared biology. The toxoplasma's complement of purine salvage enzymes is remarkably varied [13].

The purine salvage routes of toxoplasma gondii are redundant, allowing it to use the majors in the host tissue, adenosine or hypoxanthine. Toxoplasma gondii does not require either adenosine kinase (ak) or hypoxanthine quinine phosphoriboysl transferase (hxgprt), but both genes cannot be mutated at the same time. Although *T. gondii* also possesses uracil phosphoriboysl transferase (uprt), it seems to need its pyramidine biosynthesis enzymes for replication and pathogenicity, likely due to the low exogenous pyrimidine levels that support rapid cell division [19].

Potential Drug Targets for Chemotherapy in Toxoplasma: Because of its distinct structure and function in comparison to their native home, the parasite's mitochondrion is the most valuable and promising organelle for chemotherapeutic drugs. Actually, compared to their host species, protozoa's (toxoplasma) respiratory systems usually exhibit a wider variety of electron pathways. These distinctive features of the etc complex and the enzymes that are associated with them make them attractive targets for chemotherapy [17].

Targeting Metabolic Processes for Chemotherapeutics (Chemotherapy): The ability of toxoplasma to transform biochemical substances into products that support the parasites' growth and survival is indicated by its metabolism. Enzymes catalyze a sequence of biological processes that result in a sophisticated and intricate metabolic network.

These reactions are arranged into metabolic pathways. Highly specialized pharmacological chemicals can target a crucial enzyme in this metabolic network to limit cell growth; this process is responsible for a significant number of currently available medications. Targeting enzymes that lack a host homologue and that the drug may inhibit due to a lack of specificity is a typical strategy in the context of anti-pathogen medicine [20].

The core energy metabolism of apicomplexan parasites, such as toxoplasma gondii, is primarily mediated by dehydrogenases and mitochondrial redox-related activities. New methods of controlling parasites use these enzymes and pathways as target areas. Potential therapeutic targets include some dehydrogenases of the tricarboxylic acid (tca) cycle of apicomplexan parasites and the mitochondrial enzymes of the etc, as currently understood [21].

Drug resistance has significantly reduced the range of available treatments for toxoplasmosis (protozoal parasites) in recent years. In particular, mutations in the etc cytochrome b gene or alterations in iron homeostasis caused by the mitochondrial enzyme aconitase alter the sensitivity of multi-drug resistance (mdr) and control the level of resistance to anti-parasitic medications. The primary target of the medication is a cytochrome independent aox in the parasite. The majority of secretary proteins are produced as preproteins that are directed to the er, the secretory system's entrance, by a hydrophobic n-terminal signal sequence. Although t. Gondii has a typical amino acid (peptide) signal sequence, signal peptidase is not thought to be a good target for drug discovery because it is highly conserved among eukaryotes [22].

One possible target for preventing t. Gondii cell invasion and replication is the protease involved in t. Gondii invasion. The apicoplast is a plastid-like organelle seen in *T. gondii* and other apicomplexan parasites. This is a significant possible therapeutic target. Since the fatty acid production pathway of t. Gondii is essential to the protozoans' survival, apicoplast-associated enzymes are used as possible therapeutic targets. The fold-based recognition method was used to predict the structure of the drug target protein. Finding new therapeutic chemicals that can effectively combat toxoplasmosis involves screening functional inhibitors against this novel target [23]. For the synthesis of nucleic acids, they need a lot of purine and pyrirnidine nucleotides. Therefore, purine and pyrimidine anti-metabolites that impede nucleotide synthesis should also inhibit parasite reproduction [24].

Chemotherapy of Toxoplasmosis: The main treatment for illnesses caused by protozoal parasites is chemotherapy. In fact, this strategy is used in the current toxoplasmosis treatment, which inhibits nucleotide synthesis by limiting t. Gondii's folate metabolism. There are hundreds of purine and pyrimidine analogs that can be used as possible

chemotherapeutic drugs to treat toxoplasmosis. However, a thorough understanding of the enzymatic processes involved in t. Gondii's nucleotide production is necessary to pinpoint possible targets for these substances. Chemotherapy is the primary treatment for diseases brought on by protozoal parasites. The current treatment for toxoplasmosis actually employs this tactic, which restricts *t. Gondii's* folate metabolism in order to prevent nucleotide synthesis. For the treatment of toxoplasmosis, hundreds of purine and pyrimidine analogs may be employed as potential chemotherapeutic medications. To identify potential targets for these compounds, however, a detailed knowledge of the enzymatic mechanisms behind *T. gondii's* nucleotide synthesis is required [17].

For diseases brought on by protozoal parasites, chemotherapy is the primary treatment. This approach, which restricts t. Gondii's folate metabolism, is actually employed in the current toxoplasmosis treatment, which limits nucleotide synthesis. The treatment of toxoplasmosis may involve the use of hundreds of purine and pyrimidine analogs as potential chemotherapeutic medications. However, identifying potential targets for these compounds requires a detailed knowledge of the enzymatic mechanisms behind t. Gondii's nucleotide synthesis [25].

Chemotherapy is used to treat diseases brought on by protozoal parasites. This method, which restricts t. Gondii's folate metabolism, is actually employed in the present treatment for toxoplasmosis in order to prevent nucleotide synthesis. Hundreds of purine and pyrimidine analogs are available for potential use as chemotherapeutic medications to treat toxoplasmosis.

Identification of potential targets for these compounds, however, requires a detailed knowledge of the enzymatic mechanisms behind t. Gondii's nucleotide synthesis [5].

Chemotherapy is the primary treatment for disorders brought on by protozoal parasites. Actually, the current treatment for toxoplasmosis employs this tactic, which restricts t. Gondii's folate metabolism in order to prevent nucleotide synthesis. Toxoplasmosis can be treated with a variety of chemotherapeutic medications, including hundreds of purine and pyrimidine analogs. However, to identify potential targets for these compounds, a detailed knowledge of the enzymatic mechanisms behind *T. gondii's* nucleotide synthesis is required [26].

Pregnant ladies were occasionally treated with it. Systemic toxoplasma infection in dogs and cats is treated with oral doses of 30 mg/kg sulfa and 0.25 to 0.5 mg/kg pyrimetamine twice daily for two weeks. The folate biosynthesis pathway, which is lacking in human metabolism, is the focus of current medication treatments for toxoplasmosis [17]. Furthermore, more than half of the patient's experience the toxicity of this medication, which includes severe skin rashes and bone marrow suppression and in many cases, the treatment needs to be stopped [27].

However, because of their comparable mechanisms of action, people who are tolerant of pyrimethamine and sulfamethoxazole are typically intolerant of this treatment as well. The synergistic activity of trimethoprim with a sulfonamide (sulfamethazole) results in a cidal effect. The preferred therapy for toxoplasmic encephalitis in aids patients are pyrimethamine and sulfadiazine.for one to two weeks, cats may receive treatment to control oocyst darkening at a rate of 100 mg/kg. Monensin is an ionophoric coccidiostat that can be added to cat food at a dry matter rate of 0.2% for 1-2 weeks to reduce toxoplasma occyst shedding [25].

CONCLUSION AND RECOMMENDATIONS

A global zoonotic disease, toxoplasmosis poses a serious threat to both human and veterinary health. In humans, serious illnesses have been noted in immunocompromised people, including aids patients and congenitally infected children. Farmers, slaughterhouse employees and veterinarians who handle contaminated materials run the risk of contracting the disease at work. Transmissions include mother-to-child (congenital), animal-to-human (zoonotic) (undercooked meat) and food-borne (by consuming oocysts). Drug resistance significantly reduces the range of accessible medications to treat toxoplasmosis and the medications now used to treat toxoplasma infections have serious side effects and are poorly tolerated. To find possible pharmacological targets, a lot of studies have been done all across the world. These studies found 29 enzymes that are present in toxoplasma gondii but not in humans, which are distinct within shared pathways under the categories of energy metabolism, carbohydrate metabolism, nucleotide metabolism and amino acid metabolism. The latter are being investigated in detail as possible targets for chemotherapeutic treatment.

Based on the above conclusion the following recommendations are forwarded:

- Pregnant women should avoid contact with any possible source of infection, such as undercooked meat or cat faces and public education should be provided.
- When handling infectious material, veterinarians and farm workers should take steps to prevent infection, especially if they are pregnant or have weakened immune systems.
- Toxoplasma metabolic enzymes must be the target of new treatment formulations (drug design) due to medication resistance and side effects.
- Combination therapy, rather than single therapy, should be used to treat congenitally infected children and immuocompromised individuals, including aids patients.
- The search for new drug targets should be intensified, with a focus on the metabolic enzymes specific to toxoplasma, as therapeutic agents targeting them will not affect host metabolism.

REFERENCES

1. Radostits, O.M., D.C. Blood, C.C. Gay, K.W. Hinchliff and P. D. Constable, 2007. Veterinary medicine, a text book of cattle, horse, pigs, sheep and goats, 10th ed., London Saunders Elsevier, pp: 120-1206.
2. Dubey, J. P. and C.P. Beattie, 1998. Toxoplasmosis in animals and man. Journal of Medicine, 1: 45-46.
3. Krauss, H., A. Weber, W. Applel, B. Enders, H.D. Isenberg, H.G. Schefer, W.S. Sneczka and A.V. Graevenith, 2003. Zoonosis Infectious Disease Transmissable from Animal to Human. 3rd ed. Washington DC. Asm Press, pp: 307-312.
4. Parija, S.C., 2003. Medical parasitology, protozoology and helmontology (text and color atlas).India. AIPD, Regdd, Chunnai New Delhi, pp: 172-179.
5. Djurkovic-Djakovic, O., V. Milenkovic, A. Nikolic and B. Bobic, 2002. Efficacy of atovaqaone combination with clindamycine in *T. gondii*. J. Anti-microbial Chemotherapy, 56: 981-7.
6. Sunder, N., J.P. Dubey, D. Hill, G.V. Murogan, A. Bandinil, O.C. Kwok and D.S.U.C. Majiudar, 2008. High prevalence and abundant atypical genotype of Toxoplasma gondii isolated from lambs defined for human consumption USA. International Journals, 1: 145-151.
7. Urquhart, G. M., J.J. Armor, A.M. Dunn and F.W. Jennings, 1996. Veterinary Parasitology. 2nd ed. Black Well Science LTD, pp: 2357-8.
8. Acha, P.N. and B.B. Szyfre, 2003. Zoonosis and communicable disease common to man and animal. 3rd ed, Washington DC: Black Well Science, pp: 76-81.
9. Jones, J.L. and J.P. Dubey, 2012. Food born toxoplasmosis 'clinical infection diseases. An official publication of the infectious diseases society of America, 55: 845-51.
10. Astrid, H., A. Tenter, M. Anja, R. Heckeroth and M.W. Louis, 2011. Toxoplasma gondii from animal to human. International Journal of Parasitology, 30: 1217-1258.
11. Michael, W.B. and C.B. John, 2004. Life cycle of Toxoplasma gondii, Microbial molecule. Journal of Biol. Rev., 56: 607-675.
12. Gaskell , E.A., J.E. Smith, J.W. Pinney, D.R. Westhead and G.A. McConkey, 2009. A unique dual activity amino acid aydroxylase in Toxoplasma gondii. PLoS ONE, 4(3): e4801.
13. Donald, R.G.D., B. CarterUliman and D.S. Roos, 1996. Biological chemistry of Toxoplasma gondi cloning and gene expression. Journal of Molecular Biology, 171: 1401-9.
14. Huang, J., N. Mullapudi, Z. Sicherit, T. Ponten and J. C. Kissinger, 2004. Pattern and gene transfer in Apicomplexa. International Journal of the Parasitol., 1: 215.
15. Denton, H., C.W. Roberts, J. Alexander, K.W. Thong and G.H. Coombs, 1996. Enzyme of Energy Metabolism in Bradyzoites and Tachyzoites of *Toxoplasma gondii*. Institution of Biomedical and Life science, 137: 103-8.
16. Tonkin, M.L., O. Gruj, M. Pearce, J. Crawford and M. Boulanger, 2010. Molecular biochemistry and microbiology. Journal of Molecular Biology, 19: 1985-90.
17. John and D. Boothroyd, 2009. Molecular genetics, biochemistry and pharmacology. Journal of Medical and Life Science, 1: 325-327.
18. Thaimattam, R., R. Banerjee and R. Miglani, 2007. Molecular modeling and Drug design. Journal of Parasitology, 13: 2751-65.
19. Chaudhary, K., B.A. Fox and D.J. Bzik, 2002. Denovo pyrimidine biosynthesis is required for virulence of *Toxoplasma gondii*, comparative aspect of nucleotide and aminoacid metabolism: Intrnational Journals, 451: 926-929.

20. Striepen, B., A.J.P. Pruissers, J. Huang, M.J. Gubbesls, N.N. Umejiego, L. Hedstron and J.C. Kissinger, 2004. Genetic complication in apicomplexan parasites. Proc. Natl. Acad. Sci., 99: 6304-6309
21. Michael, W., B. Matherkarl, W. Henry and B.V. Akhil, 2007. Department of microbiology and immunology, International Journals of Parasitol, 8: 45-72.
22. Greene, E.E., 2006. Infectious diseases of the dogs and cat. 3rd ed. Saunder Elsevier, pp: 754-764.
23. Vanreken, D.E. and R.D. Person, 1990. Anti-parasitic agent principal and practice of infectious disease, 3rd ed. New York, pp: 398-427.
24. John, H.E., 2007. Bioscience (Targeting purine and pyrimidine metabolism in human Apicomplexan parasites. Faculty of Bioscience UK, 8: 31-47.
25. Boothe, D.M., 2001. Small animal clinical pharmacology and therapeutics. 9th ed. USA. W.B. Saunders Company, pp: 261-264.
26. Agarwal, S.L. and A. Sunil, 2007. Pharmacology for undergraduates. 2nd ed, London: Black Well Science, pp: 248-353.
27. Flegr, J., 2013. Influence of latent Toxoplasma infection on human personality, physiology and morphology pros and cons of the Toxoplasma human model the Journal Experimental Biology, 216: 127-33.