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HISTOPATHOLOGICAL FINDINGS OF LYMPHOID ORGANS DUE TO ADMINISTRATION OF LONG ACTING OXYTETRACYCLINE FORMULATION IN RATS

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Abstract: The role of immune system is to sustain host defense mechanisms and maintain homeostasis. The immune system maintains a constant surveillance against invading pathogenic microorganisms, Immunomodulation may involve either an increase in the magnitude of immune response i.e. immunostimulation or a decrease in the magnitude of the immune response i.e. immunosuppression. Long acting oxytetracycline broad spectrum antibiotic with bacteriostatic activity widely used in veterinary medicine for the treatment of respiratory and gastrointestinal infectious diseases. This study the effect of long acting oxytetracycline on immune response with the histopathological studies. The histopathological studies revealed normal appearance of spleen and lymphnode in long acting oxytetracycline low and high dose treated group when compared to control groups, which in concluded that the long acting oxytetracycline did not produce any toxicological findings and not affect the immune response in rats.

Keywords: Long acting oxytetracycline, histopathology, Spleen, lymphnode.

Introduction

The immune system expresses an adaptive response in all the vertebrates against invading microorganisms. The role of immune system is to sustain host defense mechanisms and maintain homeostasis. The immunomodulation by drugs and chemicals appears to have its rudimentary beginning in the use of herbs and teas (decoctions), which were used to cure several maladies in oriental cultures. In Ancient Chinese medicine, use of ginseng tea was found to have immunomodulating activity by virtue of its content of trace mineral germanium (Goodman, 1988).

In future, it is possible that immunological screening tests as an adjunct to traditional pharmacokinetic or toxicity studies which are required for safety evaluation of newer

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drugs. Immunomodulation may involve either an increase in the magnitude of immune response i.e. immunostimulation or a decrease in the magnitude of the immune response i.e. immunosuppression.

Long acting oxytetracycline belongs to tetracycline group of antibiotics. It was isolated from *Actinoomycete Streptomyces rimosus.* It is broad spectrum antibiotic with bacteriostatic activity widely used in veterinary medicine for the treatment of respiratory and gastrointestinal infectious diseases. It is active against aerobic gram positive and gram negative bacteria, rickettsia, mycoplasma and chlamydial infections. The long acting formulation of oxytetracycline is the drug of choice for the treatment of acute diseases as well as supportive therapy and prophylaxis like anaplasmosis, babesiosis, theilariosis, pasteurellosis, bovine kerato conjunctivitis, ovine foot rot etc.

The pharmacokinetic parameters and the pharmacological effects of long acting oxytetracycline on various system in the body have been studied, however adequate information is not available regarding the effect of long acting oxytetracycline on the natural host defense mechanisms and specific immune response in rats. The present study was conducted to study the effect of long acting oxytetracycline on immune response with the histopathological studies.

Materials and methods

The present study was designed to evaluate the effect of long acting oxytetracycline on the innate immunity i.e., natural host defense mechanisms in normal non antigen stimulated rats and immune response in antigen stimulated rats.

Experimental animals

Wister Albino rats aged between two to three month old within body weight ranging from 150 to 200 g were procured from Small Animal House, Veterinary college, UAS, Bangalore. The animals were divided into eight experimental groups consisting of ten animals each group with equal number of male and female rats. Animals were housed in standard polypropylene rat cages and allowed for acclimatization for one week before the start of actual study and maintained hygienically under standard laboratory conditions (Alastrain and Warden, 1989), by providing commercial pellet feed and water *ad libitum*.

Drug

Long acting oxytetracycline available as Oxytetracycline dihydrate injectable solution / L.A. (Oxytetracycline dihydrate 200 mg/ml in 2-pyrrolidone) manufactured by Pfizer Limited, Mumbai was used in the experiment.

This preparation was further diluted with 2-pyrrolidone and a single administration to experimental animal by intramuscular route was carried out. Sheep red blood cell (sRBC) was used as the antigen. Sheep blood was collected in Alsever's solution and stored at 4^0C for one week then washed three times in pyrogen free sterile normal saline and two per cent sRBC suspension was prepared at the time of administrations (Shah and Gupta, 1998). The two dose level i.e. low dose and high dose were selected in the present study.

The therapeutic dose 20 mg/kg body weight used in animals was considered as low dose (Musser *et al*., 1996). Twice the concentration of therapeutic dose i.e. 40 mg/kg bodyweight was considered as high dose.

Experimental protocol

The animals were divided into eight experimental groups. The details of the treatments given were as follows.

Group I Saline control (no treatment),

Group II Vehicle control i.e. 2-pyrrolidone (0.5 ml) administered through intramuscular route.

Group III Single dose administration of long acting oxytetracycline at 20 mg/kg body weight through intramuscular route

Group IV Single dose administration of long acting oxytetracycline at 40 mg/kg body weight through intramuscular route.

Group V Administered 0.4 ml antigen on Day 0 and Day 7 intraperitonaelly.

Group VI Administered 0.4 ml antigen on Day 0 and Day 7 intraperitoneally and 0.5 ml 2-pyrrolidone through intramuscular route.

Group VII Administered 0.4 ml antigen on Day 0 and Day 7 intraperitoneally and long acting oxytetracycline at 20 mg/kg body weight through intramuscular route.

Group VIII Administered 0.4ml antigen on Day 0 and Day 7 intraperitoneally and long acting oxytetracycline at 40 mg/kgbody weight through intramuscular route.

At the end of the experimental period of six weeks, the animals were sacrificed and observed for gross lesions of internal organs. The spleen and lymph node were separated from adhering tissue using normal saline and collected by placing on blotting paper and gently pressed to remove excess of saline.

Spleen as well as lymphnode were then preserved in neutral buffered formalin for histopathological study. The tissues were processed according to the standard

histopathological procedures, then sections of 5 micron were cut and stained with Haemotoxylin and Eosin (H & E 125) (Luna, 1968).

Histopathological examination of spleen and lymphnode were conducted to evaluate the effect of long acting oxytetracycline on immune response in rats.

Results and Discussion

Spleen and lymphnode of rats administered long acting oxytetracycline alone without antigen (Group III and IV) and the antigen plus long acting oxytetracycline in low and high dose groups (Group VII and VIII) did not show any changes in spleen and lymphnode when compared to their respective control groups (Group I, II, V and VII) But, there was no study regarding the effect of long acting oxytetracycline on lymphoid organ in rats.

On the contrary, Tong *et al*. (2002) reported that long term administration of chlortetracycline at 150 mg/kg body weight showed significant inhibitory effect on T, B cell proliferation in spleen, bursa and thymus immune organs in broiler birds.

Conclusion

The histopathological studies revealed normal appearance of spleen and lymphnode in long acting oxytetracycline low and high dose treated group when compared to control groups, which in concluded that the long acting oxytetracycline did not produce any toxicological findings and not affect the immune response in rats.

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LEGENDS

Fig 1: Section of spleen showing normal distribution of red and white pulp in saline control rat

Figure 2: Section of spleen showing normal distribution of red and white pulp in pyrrolidone control rat

Figure 3: Section of spleen showing normal distribution of red and white pulp in long acting oxytetracycline high dose injected group

Figure 4: Section of spleen showing normal distribution of red and white pulp in antigen control rat

Figure 5: Section of spleen showing normal distribution of red and white pulp in antigen and pyrrolidonecontrol rat

Figure 6: Section of spleen showing normal distribution of red and white pulp in antigen and long acting
oxytetracycline high dose injected rat

Figure 7: Section of lymphnode showing normal distribution of lymphocyte in cortex and medulla in saline control rat

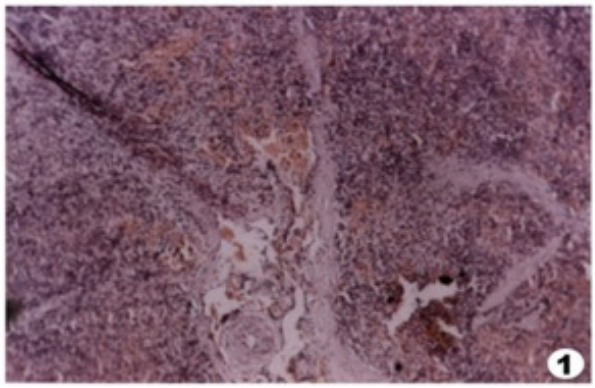
Figure 8: Section of lymphnode showing normal distribution of lymphocyte in cortex and medulla in pyrrolidone control rat

Figure 9: Section of lymphnode showing normal distribution of lymphocyte in cortex and medulla in long acting oxytetracycline high dose injected group

Figure 10: Section of lymphnode showing normal distribution of lymphocyte in cortex and medulla in antigen control rat

Figure 11: Section of lymphnode showing normal distribution of lymphocyte in cortex and medulla in antigen and pyrralidone control rat

Figure 12: Section of lymphnode showing normal distribution of lymphocyte in cortex and medulla in antigen and long acting oxytetracycline high dose injected rat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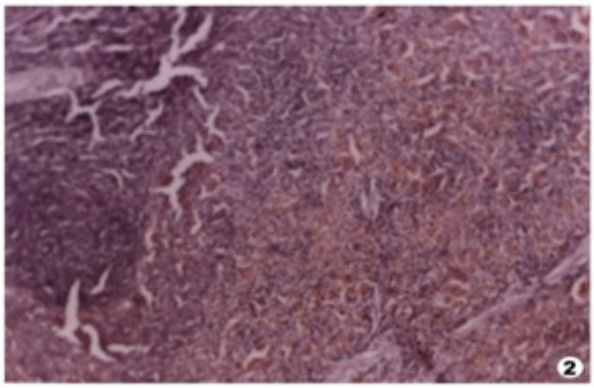
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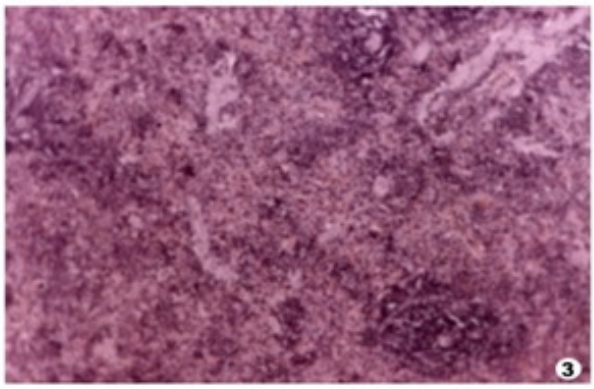
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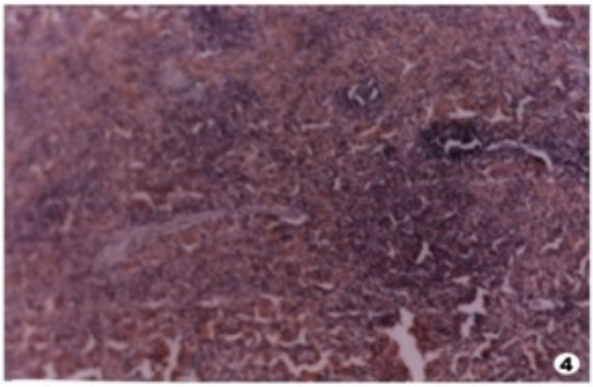
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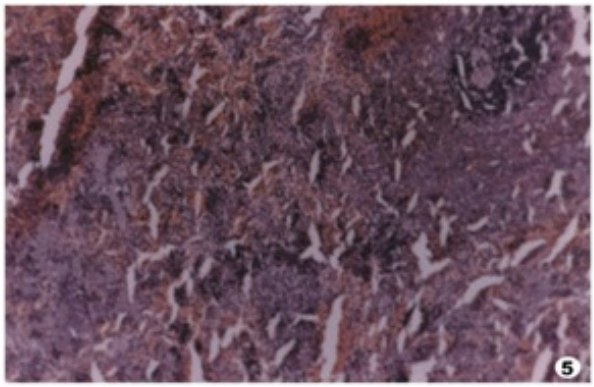
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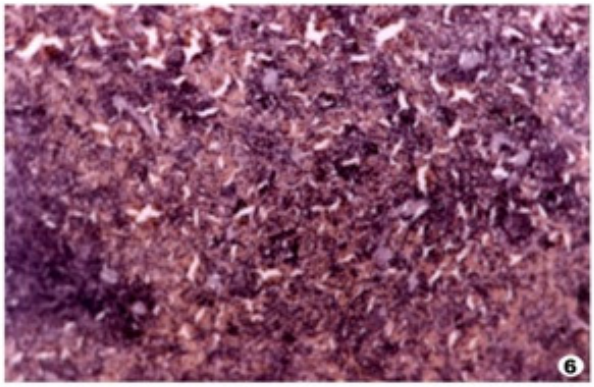
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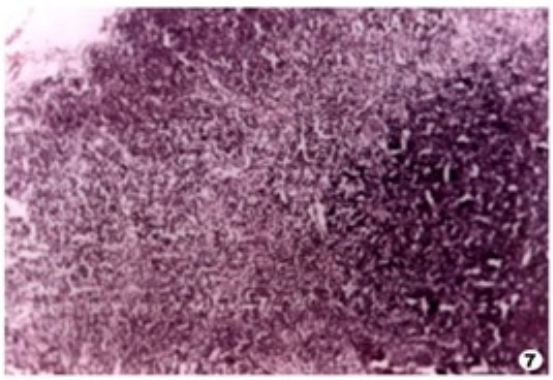
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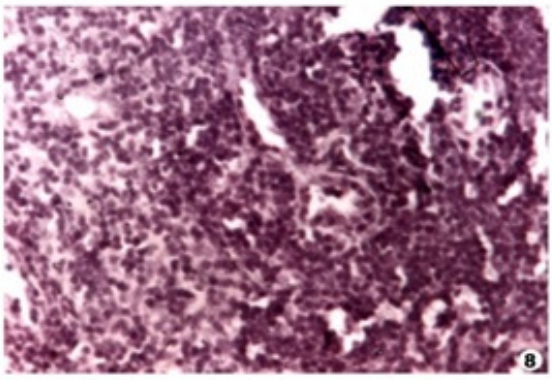
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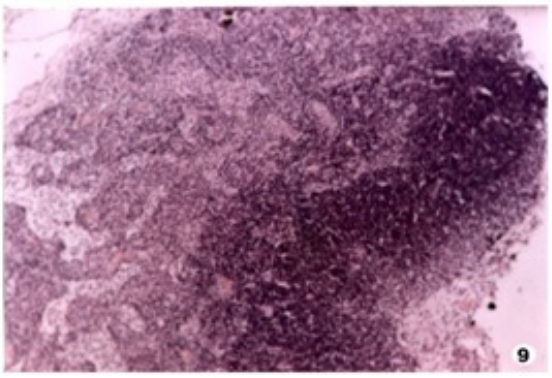
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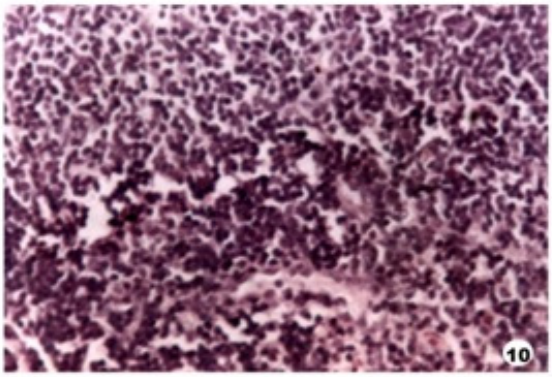
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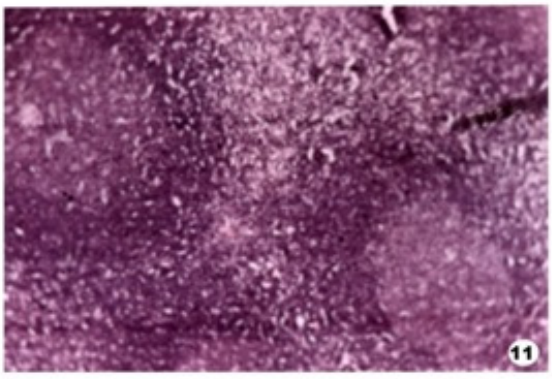
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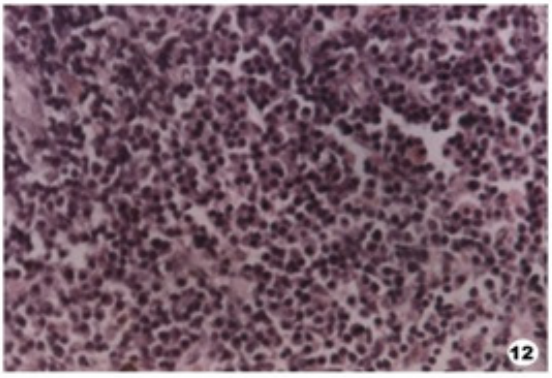
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