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# The Effects of Lindane on Rabbit Hemopoietic System: An Experimental Study

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Lindane is a synthetic insecticidal agent used in agricultural as well as medical practice. In this experimental study, effects of lindane were observed on bone marrow in rabbits. Ninety rabbits were divided in nine groups according to dose level. Low peripheral blood counts and suppression of bone marrow were observed in six test animals. This suppression was related neither to dose nor to duration of exposure to lindane.

**Keywords:** Lindane, Erythropoiesis, Myelopoiesisis, Megakaryocytes

## Introduction

Lindane is the commercial name given to the pure gamma isomer of chlorinated hydrocarbon insecticide Benzene Hexachloride. Although insecticidal use of lindane began in 1942, the suppressive effect of lindane on hemopoietic system was first reported in 1953. Further studies revealed that lindane causes injury at the level of bone marrow.[1] According to a detailed report in 1965 lindane was suggested as a possible etiologic agent responsible for various cases of bone marrow suppression.[2] Other workers have also described lindane to be directly or indirectly responsible for several cases of blood dyscrasias.[3] According to a report published by WHO in 1975, 79 persons exposed to lindane were studied, in which no evidence of bone marrow suppression was found[4]. In 1989 cases of bone marrow suppression were reported. In all these cases there was a definite history of exposure to lindane.[5] Lindane is also used for pediculosis capitis or pubis. For this purpose it is available as a shampoo, lotion or cream. Concerns about hematotoxicity have resulted in warnings that lindane should be used with caution in infants, children and pregnant women.[6] This experimental study was undertaken in order to observe the effects of orally administrated lindane on hemopoiesis in rabbits.

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## Materials and Methods

A total of 90 healthy domestic adult rabbits were used as experimental animals. They were divided into nine groups. Ten animals were included in each group. Group 1 served as normal control. The remaining eight groups were test groups at different dose levels as shown in Table 1.

**Table 1. Dose Levels of Lindane for Different Groups of Rabbits**

| Groups | Dose Level |
|---|---|
| I | Control |
| II | 5 mg/kg body weight |
| III | 10 mg/kg body weight |
| IV | 15 mg/kg body weight |
| V | 20 mg/kg body weight |
| VI | 30 mg/kg body weight |
| VII | 60 mg/kg body weight |
| VIII | 90 mg/kg body weight |

| | |
|---|---|
| IX | 120 mg/kg body weight |

**Adjustment of Highest Dose:** LD-50 of lindane for different animals in oral administration is 25-200 mg/kg body weight.[7] In order to prevent animal death due to over dosage, highest dose was kept at 120mg/kg body weight.

**Preparation of Dose:** Since lindane is readily absorbed from alimentary canal when dissolved in corn oil the respective dose for each group was given orally once a day.

**Collection of Samples:** First samples were collected at the end of second week. Sampling was repeated at an interval of two weeks till the end of sixteenth week.

Blood samples were collected from medial peripheral vein of rabbit ear by venepuncture. For the collection of bone marrow samples animals were anaesthetised by open ether anaesthesia. The skin and muscles overlying femur were incised and upper end of femur was exposed. The femur was resected, and bone marrow taken out to prepare smears on clean glass slides. Animals were sacrificed after collection of samples.

**Investigations**: Following investigations were performed in accordance with the recommended procedures: Haemoglobin level, Reticulocyte count, Platelet count, Total leukocyte count, Differential leukocyte count and Bone marrow examination.

## Results

Observations on animals of test groups were compared with control group animals. In total, six test animals showed suppression of bone marrow. Table 2 shows peripheral blood counts in rabbits showing bone marrow suppression.

Six test animals showed hypoplastic marrows. At the end of sixth week of lindane administration, one test animal each receiving doses of 60 mg/kg body weight., 90 mg/kg body weight and 120 mg/kg body weight revealed hypoplastic marrows. There was suppression of erythropoiesis, myelopoiesis as well as megakaryocytes. Lymphocytes were prominent when compared with marrow smears of control animal.

At the end of tenth week of lindane administration, one test animal each at dose levels of 5 mg/kg body weight and 20 mg/kg body weight showed marrow smears which were hypoplastic. Hypoplasia involved both erythropoiesis as well as myelopoiesis. Megakaryocytes were reduced and lymphocytes were prominent when compared with marrow smears of control animal.

At the end of fourteenth week of lindane administration, one test animal receiving the dose of 20 mg/kg body weight revealed hypoplastic marrow smears. Erythropoiesis as well as myelopoiesis were hypoplastic. Megakaryocytes were reduced in number. Lymphocytes were prominent when compared with marrow smears of control animal.

## Discussion

A number of cases with low peripheral blood counts and suppression of bone marrow were mentioned in WHO data sheet on pesticides in 1975.[4] There was a history of exposure to lindane. Blair et al also made similar observations in 1985.[8] In our study low peripheral blood counts were observed in 6 test animals.

Many workers have reported bone marrow suppression in cases with history of exposure to lindane.[9-12] In our study test animals showing low peripheral blood counts also showed suppression of erythropoiesis, myelopoiesis and megakaryocytes in the bone marrow. In this study the bone marrow smears of animals at all dose levels were compared with the bone marrow smears of normal control animal.

As a result of this experimental study it can be concluded that lindane caused suppression of bone

**Table 2: Peripheral Blood Values in Rabbits showing Bone Marrow Suppression**

| Weeks | Dose Levels (mg/kg) | Hb (gm/dl | Retic (%) | Platelets ($X10^9$/1) | TLC (/cmm | Leukocyte Absolute Counts (Per cmm) |
|---|---|---|---|---|---|---|

| | | ) | | | ) | N | L | M | E |
|---|---|---|---|---|---|---|---|---|---|
| 6th | 60 | 8.7 | 2.0 | 20 | 1900 | 57 | 1843 | 0 | 0 |
| 6th | 90 | 8.0 | 0.5 | 110 | 1200 | 48 | 1128 | 0 | 24 |
| 6th | 120 | 9.2 | 1.5 | 45 | 700 | 14 | 672 | 14 | 0 |
| 10th | 05 | 8.0 | 2.0 | 60 | 2000 | 180 | 1820 | 0 | 0 |
| 10th | 20 | 8.0 | 2.0 | 100 | 2100 | 168 | 1932 | 0 | 0 |
| 14th | 20 | 8.0 | 1.0 | 27 | 1100 | 33 | 1067 | 0 | 0 |

marrow in test animals. This was related to individual susceptibility of the rabbits. No relationship was found either with dose or duration of exposure to lindane.

Experimental studies at best can provide only an indication of the type of damage which may be expected. Intensive studies and reporting of human cases should be undertaken whenever circumstances permit It is therefore recommended that indiscriminate use of lindane be prevented. Proper preventive measure should be taken by those exposed to lindane and other insecticides either at home or in agricultural practice. The continuous extravagant promotion of certain types of insecticides is also of great importance to those responsible for protection of public health.

The mechanism of bone marrow suppression due to various chemicals and drugs is two fold. Firstly, it can occur as a result of direct toxic effect on pleuripotent haemopoietic stem cells. In this case the marrow suppression is usually reversible on cessation to exposure. However, exposure to exceptionally high dose may result in myeloablation which may be irreversible. Secondly, myelosuppression may occur as a result of idiosyncrasy or hypersensitivity. This reaction is not dose related and is usually irreversible.[12]

In the present study, lindane-induced myelosuppression was probably not dose related. It was observed at 6th week in only 10% of the groups of animals, which were given 80mg, 90mg or 120mg/kg of lindane. The comparison among these groups with controls and the remaining five groups was insignificant ($p > 0.05$). After 10 weeks, 10% each of animals groups receiving 5mg/kg and 20mg/kg lindane showed pancytopenia as a result of myelosuppression. At 14 weeks, another 10% of the group receiving 20mg/kg lindane developed pancytopenia, making total affliction of 20% in this group.

In all the six animals, which developed bone marrow suppression, the first evidence of marrow failure was pancytopenia. The marrow suppression was later confirmed by bone marrow biopsy. It can be hypothesized that during the lag period of six to fourteen weeks, either cumulative effect of the drug occurred or myelosuppression resulted from hypersensitivity. It is proposed that further experimental studies should be undertaken to resolve this question.

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