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From: Ind Vet Journal (ivj83@yahoo.com)

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Date: Monday, July 1, 2019 at 03:30 PM GMT+7

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### **ACKNOWLEDGEMENT**

Reg. No: 249/19

Dated : 1/07/2019

**Dear Dr.** Erma Safitri,

We acknowledge the receipt of the following articles entitled "Immunomodulatory activity of black jinten oil (*Nigella sativa*) as macrophage activator for *Salmonella typhimurium* infected rat." (Erma Safitri, *et al.*).

For any further correspondence, please always quote the Registration Number of the Article.

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On Saturday, 29 June 2019, 10:28:44 am UTC, Safitri Erma <rma\_fispro@yahoo.com> wrote:

Date, 29 June 2019

Dear Editor Indian Veterinary Journal

I hereby send our manuscript research article with the tittle :

**Immunomodulatory activity of black jinten oil (*Nigella sativa*) as macrophage activator for *Salmonella typhimurium* infected rat**

**Keywords :** Black jinten oil, Immunomodulators, Leukocytes, Macrophage, Salmonellosis.

The article we sent has not been previously submitted and has not been submitted for evaluation in other journals.

Please submission our article for published in Indian Veterinary Journal

Thank you

Best Regard,

Corresponding Author,

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## Article # 249/19 for revision and referee comments attached.

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From: Ind Vet Journal (ivj83@yahoo.com)  
To: rma\_fispro@yahoo.com  
Cc: dewa.meles@yahoo.co.id  
Date: Saturday, August 24, 2019 at 05:17 PM GMT+7

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Sir / Madam,

Revise the paper according to the referee's comments and corrections marked on the manuscript. Resubmit the revised article as per IVJ format for further action.

Sincerely

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# THE INDIAN VETERINARY JOURNAL

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ARTICLE NO: 249/19

Date: 19.8.19

### Author is requested to note :

- Revise the paper according to the referee's comments and corrections marked on the manuscript.
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- Resubmit the revised article as per IVJ format – one hard copy and one soft (CD) for each article separately.

### EDITOR's COMMENTS

- 1) Abstract should not exceed 100 words -
- 2) Results and discussion to be abridged and presented
- 3) Mistakes in the references section may be rectified
- 4) Mean and S.E. to be furnished in the tables -
- 5) Corrections/deletions/additions/suggestions pointed out may be carried out and revised article submitted as full research article not exceeding 6 pages, inclusive of tables, ~~for~~ after going thro' the enclosed IVJ guidelines for further action

To  
..... Dr. Emma Sabitri .....

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249/19  
II

## Immunomodulatory activity of black jinten oil (*Nigella sativa*) as macrophage activator for *Salmonella typhimurium* infected rat

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### Abstract

This study was aimed to prove immunomodulatory activity of black jinten oil (*Nigella sativa*) as macrophage <sup>activator</sup> for *Salmonella typhimurium* infected rat. 125<sup>th</sup> rats were divided <sup>into</sup> 5<sup>th</sup> groups <sup>and</sup> 5<sup>th</sup> days observation <sup>at</sup> (2<sup>nd</sup>, 4<sup>th</sup>, 6<sup>th</sup>, 8<sup>th</sup> and 10<sup>th</sup>). The treatment group <sup>was</sup> were infected with *Salmonella typhimurium* 10<sup>5</sup> CFU intraperitoneal. Furthermore, the treatment group <sup>was</sup> were given black jinten oil dose: 12.60 mg, 18.90 mg and 25.20 mg per 200 gram bw/day for 10 days. The parameters were observed: total number <sup>of</sup> leukocytes, neutrophils, eosinophils, basophils, lymphocytes, monocytes and activated macrophages. The results were obtained of black jinten oil to be able for maintaining an immune response towards normal total number of leukocytes and activated macrophages, in rats <sup>which</sup> were infected with *Salmonella typhimurium*.

**Keywords** : Black jinten oil, Immunomodulators, ~~Leukoocytes~~, ~~Macrophage~~, Salmonellosis

Black jinten oil (*Nigella sativa*) is natural immunomodulator and often used to strengthen the immune system from attacks by viruses, germs, bacteria and extreme changes in conditions. Jinten seed oil contains a number of chemicals that have activities as hypo-allergenic, antiprostaglandin, antihistamines, anti-inflammatory and immunodeficiency (Akpolat and Kanter, 2009). So that it can be used as a medicine to prevent and treat for immune deficiency such as in Salmonellosis case.

### Materials and Methode

125<sup>th</sup> rats were divided <sup>into</sup> 5<sup>th</sup> groups <sup>and</sup> 5<sup>th</sup> days observation <sup>at</sup> (2<sup>nd</sup>, 4<sup>th</sup>, 6<sup>th</sup>, 8<sup>th</sup> and 10<sup>th</sup>). The treatment group <sup>was</sup> were infected with *Salmonella typhimurium* 10<sup>5</sup> CFU intraperitoneal (Cart, 2003, Mustofa *et al.*, 2017). Furthermore, the treatment group were given black jinten oil dose: 12.60 mg (T1), 18.90 mg (T2) and 25.20 mg (T3) per 200 gram bw/day for 10 days and <sup>then</sup> were compared with control negative (C-) = healthy rats and control positive (C+) = rats with salmonellosis and without black jinten oil. The parameters <sup>were</sup> were observed: total number leukocytes, neutrophils, eosinophils, basophils, lymphocytes, monocytes and activated macrophages. ~~The results were obtained of black jinten oil to be able for maintaining an immune response towards normal total number of leukocytes and activated macrophages.~~ The ~~research data obtained~~ <sup>was</sup> were analyzed by one-way analysis. ~~if~~ there were differences, further analysis was carried out with the smallest real difference test.

Art. 249/19  
May be proceeded  
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## Results and Discussion

The results of the examination of total leukocytes, neutrophils, eosinophils, basophils, lymphocytes, monocytes and activated macrophages in rats (*Rattus norvegicus*) after infection with *Salmonella typhimurium*, then given black jinten oil extract at various doses, the results can be seen in Table 1 – 7.

*conclude the results and discussion part with salient findings and restrict the R+D part within in one page only*

Table I. Average of total leukocytes on rats administrated with black jinten oil extract after being infected with *Salmonella typhimurium* (Mean  $\pm$  S.E.?)

Treatment	Average of Total Leukocyte Count in Days				
	2nd	4th	6th	8th	10th
C-	7880 <sup>a</sup> $\pm$ 228.03	7900 <sup>a</sup> $\pm$ 158.11	7960 <sup>a</sup> $\pm$ 207.36	7860 <sup>a</sup> $\pm$ 230.21	7920 <sup>a</sup> $\pm$ 389.87
C+	13940 <sup>b</sup> $\pm$ 194.93	13820 <sup>b</sup> $\pm$ 192.35	13900 <sup>b</sup> $\pm$ 187.08	13960 <sup>b</sup> $\pm$ 89.44	13920 <sup>b</sup> $\pm$ 130.384
T1	10780 <sup>c</sup> $\pm$ 861.39	10540 <sup>c</sup> $\pm$ 746.99	10680 <sup>c</sup> $\pm$ 589.06	10220 <sup>c</sup> $\pm$ 438.17	10140 <sup>c</sup> $\pm$ 804.98
T2	7980 <sup>a</sup> $\pm$ 526.30	8040 <sup>a</sup> $\pm$ 89.44	8020 <sup>a</sup> $\pm$ 715.54	7880 <sup>a</sup> $\pm$ 356.37	7940 <sup>a</sup> $\pm$ 642.65
T3	7960 <sup>a</sup> $\pm$ 114.01	7940 <sup>a</sup> $\pm$ 650.38	7940 <sup>a</sup> $\pm$ 384.70	7800 <sup>a</sup> $\pm$ 187.08	7780 <sup>a</sup> $\pm$ 228.03

different letter superscripts in one column indicate differences ( $p < 0,05$ )

### II

Table 2. Average of Eosinophil count on rats administrated with black jinten oil extract after being infected with *Salmonella typhimurium* (Mean  $\pm$  S.E.?)

Treatment	Average of Rats Eosinophil Count in Days				
	2nd	4th	6th	8th	10th
C-	313.80 <sup>a</sup> $\pm$ 10.73	314.8 <sup>a</sup> $\pm$ 5.93	317.20 <sup>a</sup> $\pm$ 9.75	313.20 <sup>a</sup> $\pm$ 10.73	314.20 <sup>a</sup> $\pm$ 10.01
C+	556.4 <sup>b</sup> $\pm$ 10.43	552.40 <sup>b</sup> $\pm$ 8.04	55480 <sup>b</sup> $\pm$ 8.67	557.20 <sup>b</sup> $\pm$ 5.21	558.00 <sup>b</sup> $\pm$ 7.48
T1	430.0 <sup>c</sup> $\pm$ 33.16	443.40 <sup>c</sup> $\pm$ 75.78	434.00 <sup>c</sup> $\pm$ 19.79	408.40 <sup>c</sup> $\pm$ 14.44	408.40 <sup>c</sup> $\pm$ 14.44
T2	346.0 <sup>a</sup> $\pm$ 13.41	327.60 <sup>a</sup> $\pm$ 19.20	317.20 <sup>a</sup> $\pm$ 30.77	314.00 <sup>a</sup> $\pm$ 15.74	314.00 <sup>a</sup> $\pm$ 12.16
T3	321.2 <sup>a</sup> $\pm$ 7.69	318.00 <sup>a</sup> $\pm$ 23.66	316.40 <sup>a</sup> $\pm$ 14.99	310.80 <sup>a</sup> $\pm$ 7.94	309.60 <sup>a</sup> $\pm$ 5.89

different letter superscripts in one column indicate differences ( $p < 0,05$ )

### III

Table 3. Average of Basophil count in rats administrated with black jinten oil extract after being infected with *Salmonella typhimurium* (Mean  $\pm$  S.E.?)

Treatment	Average of Rats Basophil Count in Days				
	2nd	4th	6th	8th	10th
C-	77.00 <sup>a</sup> $\pm$ 5.09	77.20 <sup>a</sup> $\pm$ 3.76	77.80 <sup>a</sup> $\pm$ 5.26	78.80 <sup>a</sup> $\pm$ 5.01	76.60 <sup>a</sup> $\pm$ 5.41
C+	137.60 <sup>b</sup> $\pm$ 5.94	136.60 <sup>b</sup> $\pm$ 4.61	139.20 <sup>b</sup> $\pm$ 1.78	137.80 <sup>b</sup> $\pm$ 4.43	138.00 <sup>b</sup> $\pm$ 5.09
T1	106.00 <sup>c</sup> $\pm$ 8.94	103.60 <sup>c</sup> $\pm$ 6.50	107.00 <sup>c</sup> $\pm$ 5.65	100.60 <sup>c</sup> $\pm$ 0.54	100.60 <sup>c</sup> $\pm$ 7.43
T2	85.00 <sup>a</sup> $\pm$ 6.12	80.40 <sup>a</sup> $\pm$ 7.12	77.80 <sup>a</sup> $\pm$ 8.78	77.00 <sup>a</sup> $\pm$ 5.52	77.00 <sup>a</sup> $\pm$ 2.34
T3	78.80 <sup>a</sup> $\pm$ 258	78.00 <sup>a</sup> $\pm$ 5.91	77.60 <sup>a</sup> $\pm$ 5.59	76.20 <sup>a</sup> $\pm$ 4.43	75.80 <sup>a</sup> $\pm$ 3.56

different letter superscripts in one column indicate differences ( $p < 0,05$ )

### IV

Table 4. Average of Neutrophil count in rats administrated with black jinten oil extract after being infected with *Salmonella typhimurium* (Mean  $\pm$  S.E.?)

Treatment	Average of Rats Neutrophil Count in Days				
	2nd	4th	6th	8th	10th
C-	5034.00 <sup>a</sup> ± 198.43	5048.80 <sup>a</sup> ± 96.68	5086.40 <sup>a</sup> ± 163.20	5087.20 <sup>a</sup> ± 91.23	5074.40 <sup>a</sup> ± 128.61
C+	8914.40 <sup>b</sup> ± 140.50	8850.40 <sup>b</sup> ± 119.31	8486.80 <sup>b</sup> ± 952.45	8927.20 <sup>b</sup> ± 65.01	8940 <sup>b</sup> ± 96.41
T1	6892.00 <sup>c</sup> ± 560.64	6738.40 <sup>c</sup> ± 512.65	6956.00 <sup>c</sup> ± 320.92	6546.40 <sup>c</sup> ± 257.79	6546.40 <sup>c</sup> ± 257.79
T2	5548.00 <sup>a</sup> ± 152.05	5253.60 <sup>a</sup> ± 294.42	5138.40 <sup>a</sup> ± 482.15	5100.00 <sup>a</sup> ± 202.15	5100.00 <sup>a</sup> ± 170.31
T3	5151.20 <sup>a</sup> ± 141.77	5100.00 <sup>a</sup> ± 387.09	5138.40 <sup>a</sup> ± 178.24	5048.80 <sup>a</sup> ± 48.03	5048.80 <sup>a</sup> ± 48.03

different letter superscripts in one column indicate differences ( $p < 0,05$ )

V  
Table 7. Average of Lymphocyte count in rats administrated with black jinten oil extract after being infected with *Salmonella typhimurium* (Mean ± S.E.?)

Treatment	Average of Rats Lymphocyte Count in Days				
	2nd	4th	6th	8th	10th
C-	2034.00 <sup>a</sup> ± 106.09	2039.20 <sup>a</sup> ± 42.69	2054.80 <sup>a</sup> ± 40.51	2054.20 <sup>a</sup> ± 18.03	2049.60 <sup>a</sup> ± 20.85
C+	3609.60 <sup>b</sup> ± 83.27	3583.60 <sup>b</sup> ± 60.90	3599.20 <sup>b</sup> ± 66.50	3654.80 <sup>b</sup> ± 52.28	3620.00 <sup>b</sup> ± 63.05
T1	2788.00 <sup>c</sup> ± 244.37	2725.60 <sup>c</sup> ± 222.18	2814.00 <sup>c</sup> ± 127.87	2647.60 <sup>c</sup> ± 78.45	2647.60 <sup>c</sup> ± 138.40
T2	2242.00 <sup>a</sup> ± 56.30	2122.40 <sup>a</sup> ± 69.48	2080.80 <sup>a</sup> ± 219.20	2060.00 <sup>a</sup> ± 50.97	2060.00 <sup>a</sup> ± 50.97
T3	2080.80 <sup>e</sup> ± 41.77	2040.00 <sup>a</sup> ± 148.45	2075.60 <sup>a</sup> ± 46.65	2039.20 <sup>a</sup> ± 52.28	2023.20 <sup>a</sup> ± 71.28

different letter superscripts in one column indicate differences ( $p < 0,05$ )

VI  
Table 8. Average of Monocyte count in rats administrated with black jinten oil extract after being infected with *Salmonella typhimurium* (Mean ± S.E.?)

Treatment	Average of Rats Monocyte Count in Days				
	2nd	4th	6th	8th	10th
C=	393.00 <sup>a</sup> ± 16.43	394.00 <sup>a</sup> ± 10.24	391.00 <sup>a</sup> ± 7.58	397.00 <sup>a</sup> ± 2.73	396.40 <sup>a</sup> ± 4.09
C+	696.00 <sup>b</sup> ± 11.93	691.00 <sup>b</sup> ± 9.61	694.00 <sup>b</sup> ± 10.24	697.00 <sup>b</sup> ± 7.58	698.00 <sup>b</sup> ± 8.36
T1	538.00 <sup>c</sup> ± 41.47	526.00 <sup>c</sup> ± 36.29	543.00 <sup>c</sup> ± 24.89	511.00 <sup>c</sup> ± 19.17	511.00 <sup>c</sup> ± 19.17
T2	433.00 <sup>a</sup> ± 11.51	410.00 <sup>a</sup> ± 17.32	402.00 <sup>a</sup> ± 38.98	398.20 <sup>a</sup> ± 12.49	398.20 <sup>a</sup> ± 12.49
T3	402.00 <sup>a</sup> ± 10.36	398.00 <sup>a</sup> ± 29.91	401.00 <sup>a</sup> ± 10.24	394.40 <sup>a</sup> ± 6.22	393.40 <sup>a</sup> ± 5.45

different letter superscripts in one column indicate differences ( $p < 0,05$ )

VII  
Table 9. Average of Macrophage count on rats administrated with black jinten oil extract after being infected with *Salmonella typhimurium* (Mean ± S.E.?)

Treatment	Average of Rats Macrophage Count in Days				
	Ke 2	Ke 4	Ke 6	Ke 8	Ke 10
C-	13.20 <sup>a</sup> ± 2.16	13.40 <sup>a</sup> ± 2.07	12.80 <sup>a</sup> ± 1.30	13.40 <sup>a</sup> ± 1.94	12.80 <sup>a</sup> ± 1.30
C+	38.80 <sup>b</sup> ± 9.57	38.20 <sup>b</sup> ± 1.78	37.40 <sup>b</sup> ± 2.30	37.40 <sup>b</sup> ± 3.36	37.80 <sup>b</sup> ± 3.11
T1	26.80 <sup>c</sup> ± 5.40	27.40 <sup>c</sup> ± 2.34	27.20 <sup>c</sup> ± 1.92	27.60 <sup>c</sup> ± 4.39	26.80 <sup>c</sup> ± 4.32
T2	14.20 <sup>a</sup> ± 1.30	14.80 <sup>a</sup> ± 1.09	14.40 <sup>a</sup> ± 2.30	14.20 <sup>a</sup> ± 1.30	13.80 <sup>a</sup> ± 1.78
T3	12.80 <sup>a</sup> ± 2.38	12.60 <sup>a</sup> ± 0.54	12.60 <sup>a</sup> ± 2.79	12.40 <sup>a</sup> ± 2.30	12.20 <sup>a</sup> ± 2.28

different letter superscripts in one column indicate differences ( $p < 0,05$ )



The results of the study in rats after infection with *Salmonella typhimurium* and then administrated with black jinten oil extract, causing an increase in total leukocytes, neutrophils, eosinophils, basophils, lymphocytes, monocytes and activated macrophages. The increase in total leukocytes, neutrophils, eosinophils, basophils, lymphocytes, monocytes or activated macrophages were a mechanism of response of non-specific immunity, means the body immune responses that occur due inflammatory reactions because of stress or infections in the body <sup>which</sup> are played by leukocytes, neutrophils, eosinophils, basophils, lymphocytes, monocytes and activated macrophages.

After statistical analysis using analysis of variance (anova) on total leukocytes, neutrophils, eosinophils, basophils, lymphocytes, monocytes and activated macrophages were showed that administration of black jinten oil extract for 2 days, 4 days, 6 days, 8 days and 10 days in rats after infection with *Salmonella typhimurium* between the control negative group (C-) with the control positive group (C+) and T1 shows significant differences ( $p < 0.05$ ), while T2 and T3 <sup>showed</sup> there is no difference ( $p > 0.05$ ) with C-. This ~~was~~ showed that in rats infected with *Salmonella typhimurium* can ~~be~~ caused an increase in total leukocytes neutrophils, eosinophils, basophils, lymphocytes, monocytes and activated macrophages from infection day 2, to 4, to 6, to 8 and day 10 in C+ and T1 compared to the group of normal rats (C-).

The increase in total leukocytes in the body can be caused by several factors, such as changes in body conditions due to various causes such as prolonged stress, bacterial infections, viruses, or the entry of other foreign bodies into the body such as allergic reactions or post vaccination reactions or conditions that stimulates the emergence of inflammatory reactions in the body. Circumstances that can stimulate an increase in leukocyte levels (leukocytosis) indicate a changes in the normal body reaction to the entry of foreign material into the body including stress and infection by germs and viruses (Davis *et al.*, <sup>2008</sup> ~~loc cit~~). While the total leukocytes between the treatment control group (C+) and treatment group administrated with black jinten oil extract (T1, T2 and T3) ~~are~~ showed a significant reduction towards normal, this indicates that the administration of black jinten oil is efficacious as an immunomodulator which is able to reduce and stabilize total leukocytes of rats towards normal after infection with *Salmonella typhimurium*.

(12) Administration of black jinten oil extract at a dose of 18.90 mg / head / day in rats infected with *Salmonella* has been able to stabilize the normal body condition by maintaining the total leukocytes towards normal. The nonspecific immune response in the body can be maintained on the administration of black jinten oil fraction after infection with *Salmonella*

Compare with results



*typimurium*, means that black jinten oil extract can modulate the total leukocytes in the body towards normal and replace the role and function of leukocytes when the infection occurs in the normal direction.

Although *Salmonella* infection occurs, the administration of black jinten oil extract can stimulate the role and function of leukocytes in phagocytes process of *Salmonella typimurium* that enter the body. The leukocyte utilization in phagocytes process of *Salmonella* was induced by black jinten oil extract, for which leukocytes will be undergo programmed death through the mechanism of apoptosis because they have interacted with the infected cells. Leukocyte programmed death was mediated by the release of signaling molecules called ligands. Furthermore, the ligand will bind to the death receptor found in leukocyte transmembrane. Death receptors located on the cell surface are a family of Tumor Necrosis Factor (TNFR) receptors that initiate leukocyte death by apoptosis.

Administration of black jinten oil extract starting at a dose of 18.90 mg / head / day in rats infected with *Salmonella typimurium* was able to stabilize the body condition by maintaining the amount of Eosinophils towards normal. This means that black jinten extract is able to modulate the amount of Eosinophils in the body towards normal and replace the role and function of Eosinophils at the time of infection. The role of eosinophils will be prominently increased in parasitic infections (Hoffbrand, 2006).

The administration of black jinten extract starting from 18.90 mg / head in rats infected with *Salmonella typhimurium* has been able to stabilize the body condition by maintaining the amount of Basophils towards normal. This means that black jinten oil extract has been able to maintain the amount of Basophils in the body towards normal and replace the role and function of Basophils at the time of infection, through a decrease in the amount of Basophils aimed at rats in groups T1, T2 and T3. The amount of basophils is usually caused by myeloproliferative disorders and has an important role in hypersensitivity (Caroline *et al.*, 2009).

Black jinten oil extract administration starting at a dose of 18.90 mg / head / day in rats infected with *Salmonella* has been able to stabilize the body's condition by maintaining the amount of Neutrophils towards normal. This means that black jinten extract was able to modulate the amount of Neutrophils in the body towards normal and replace the role and function of Neutrophils at the time of infection. Neutrophils are associated with the body's defense against bacterial infections and in the inflammatory process, usually giving the first response to bacterial infections. In bacterial infections the most visible change in leukocyte

check  
Result  
in Table

changes is a significant increase in neutrophils, compared to other polymorphonuclear (PNM) leukocytes such as basophils and eosinophils (Criss *et al.*, 2001, Hoffbrand, *loc cit*).

The number of lymphocytes shows the body immune response related to the role of T cells and B cells in maintaining the body resistance if an infection occurs. T cells will differentiate into cytotoxic T cells, helper T cells, suppressant T cells, and memory T cells that play a role in the secretion of Interferon IF (IFN $\gamma$ ) in activating macrophages to phagocyte infectious microorganisms that enter the body or phagocytes infectious foreign bodies. While B cell will differentiate into memory cells and plasma cells which produced antibodies (immunoglobulins) which are humoral immune responses (Cummings, 2005; Mustofa *et al.*, *loc cit*).

Black jinten oil administration starting at a dose of 18.90 mg / head / day in rats infected with *Salmonella* has been able to stabilize the body's condition towards normal by maintaining the number of lymphocytes towards normal. This means that black jinten extract was able to modulate the number of lymphocytes in the body towards normal and replace the role and function of lymphocytes at the time of infection, but has showed a decrease in the number of lymphocytes. The immunomodulatory response displayed by black jinten oil extract is related to the increase in differentiation and proliferation activity of T cells and B cells.

Black jinten oil extract administration starting from T1 dose 12.60 mg / head / day in rats has shown a tendency to decrease the number of monocytes towards normal in rats infected with *Salmonella typhimurium* although not significant compared to normal rats, and at a dose of 18.90 mg / head / day rats infected with *Salmonella* have been able to stabilize the body condition by maintaining the number of Monocytes towards normal. This means that at a dose of 18.90 mg / head / day in rats administrated with black jinten oil extract has been able to maintain the amount of Monocytes in the body towards normal and replace the role and function of Monocytes at the time of infection.

The font can be changed to normal

Decreased macrophages towards normal numbers shows the immunological response of rats ~~bodies in phagocytes~~ <sup>and its</sup> of *Salmonella typhimurium* was added by the black jinten oil extract role in increasing the body resistance through increased polymorphonuclear such as neutrophils, basophils and eosinophils (Criss *et al.*, *loc cit*) while decreasing the number of macrophages towards normal in line with the extract dose given.

This ~~was~~ showed that the administration of black jinten oil extract after *Salmonella typhimurium* infection did not cause a significant increase in the number of macrophages



compared to normal rats. Activated macrophages play a role in phagocytes' process of microorganisms that enter the body. Activation of macrophages is very dependent on the role of T cells and B cells which differentiate and proliferate from T lymphocytes and B lymphocytes, whereas macrophages are differentiated from monocytes that enter the tissue through the process of being absorbed (Cummings, ~~loc cit~~, Mustofa *et al.*, ~~loc cit~~). The role of macrophages and activation of macrophages is very dependent on gamma interferon produced by T cells, B cells, NK cells and activated macrophage cells (Kusmardi *et al.*, 2007, Mustofa *et al.*, ~~loc cit~~). From the results of this study there was no significant difference in the number of activated macrophages, this was because the black jinten oil extract has been able to stabilize and take over the role of macrophages in maintaining immune responses, so that the results of this study concluded that black jinten extract able to act as an immunomodulator by stabilizing the immune response, although *Salmonella typhimurium* infection occurs, rats remains stable in maintaining endurance by keeping the number of macrophages remain stable after a *Salmonella* infection occurs.

Administation of black jinten oil extract with dose of 18.90 mg / head / day in rats infected with *Salmonella typhimurium* from day 2 to day 10 has been able to stabilize the body immune response by maintaining the number of macrophages towards normal. This means that black jinten oil extract able to maintain the number of activated macrophages in the body and replace the role and function of macrophages during infection by *Salmonella typhimurium*. The effectiveness of activated macrophages in phagocytes of *Salmonella* was induced by extract of black jinten oil, henceforth the activated macrophage will undergo programmed death through the mechanism of apoptosis because it has interacted with *Salmonella typhimurium* as an infected cell. The death of activated macrophages occurs programmatically mediated by the release of signaling molecules called ligands. Furthermore, these ligands will bind to death receptors found in transmembrane macrophage cells. Death receptors located on the cell surface are a family of Tumor Necrosis Factor (TNFR) receptors that initiate programmed activation of macrophages.

(Bold) Summary:

The conclusion, Black jinten oil extract can stabilize total leukocytes, neutrophils, eosinophils, basophils, lymphocytes, monocytes and activated macrophages in rats to normal direction after infected with *Salmonella typhimurium*.

**References**



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Article No.	Title	Author (s)
249/19	Immunomodulatory activity of black Jinten oil ( <i>Nigella sativa</i> ) as Macrophage activator for <i>Salmonella typhimurium</i> infected rat	Dewa K. Meles, <b>Erma Safitri</b> , Wurlina, Imam Mustofa, Suherni Susilowati Desak K.S.C. Putri

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