Effect of Cysteine Ethylester Hydrochloride (Cystanin®) on Host Defense Mechanisms (V): Potentiation of Nitroblue Tetrazolium Reduction and Chemiluminescence in Macrophages or Leukocytes of Mice or Rats

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Abstract—L-Cysteine ethylester hydrochloride (Cystanin®, ethylcysteine) at doses of 3–30 mg/kg, p.o., potentiated the reduction of nitroblue tetrazolium (NBT) by mouse peritoneal macrophages ex vivo. In in vitro experiments, this drug (30 μM) augmented NBT reduction of mouse peritoneal macrophages induced by opsonized zymosan (OZ). At the same concentration, this drug accelerated the enhancement of the OZ-induced NBT reduction by the addition of concanavalin A, N-formyl-L-methionyl-L-leucyl-L-phenylalanine or phorbol myristate acetate. This enhancing effect of ethylcysteine was completely diminished by the addition of SOD, sodium azide and catalase. In ex vivo experiments, the OZ-induced chemiluminescence of rat peritoneal macrophages and white blood cells was enhanced by the administration of ethylcysteine at doses of 3–10 mg/kg (i.p.) and 3–30 mg/kg (p.o.). In addition, this drug significantly enhanced the lumisphere-induced chemiluminescence of rat peritoneal leukocytes at 30 mg/kg (i.p.), but not the OZ-induced chemiluminescence. In in vitro experiments, this drug (30 μM) did not enhance the OZ-induced chemiluminescence response of rat peritoneal macrophages. These results suggest that ethylcysteine may enhance the intracellular generation of antimicrobial oxidants in macrophages and leukocytes.

It has been shown that L-cysteine ethylester hydrochloride (Cystanin®, ethylcysteine) potentiated both the phagocytic activity and nitroblue tetrazolium (NBT) reducing activity of rat peritoneal leukocytes (1, 2). Intracellular NBT reduction of leukocytes may be reflected in the production of intracellular high reactive oxygen radicals such as superoxide (3). Glutathione was released from proteins by cysteamine treatment (520 mM) (4), and glutathione depletion by the diethyl maleate treatment was replaced by the intraperitoneal treatment with 300 mg/kg of ethylcysteine (5). Glutathione may be important for host defense mechanisms such as the enhancement of the radioresistance of cells (4).

Tissue distribution of 35S-ethylcysteine showed high levels of radioactivity in the lung after intravenous administration, different from that observed with 35S-cysteine (6). Ethylcysteine accelerated the decrease of the viable E. coli number in the blood and liver of normal and cyclophosphamide-treated mice (7). The potentiating effects of ethylcysteine on host defenses may be partially due to the enhancement of the phagocytic activity in alveolar macrophages, monocytes and kupffer cells. In addition, there were high levels of this drug in the spleen and thymus in rats after its oral administration (8). It has been proposed that this drug can enhance the intracellular killing activity of not only peritoneal leukocytes but also macrophages of the spleen or thymus in experimental animals.

In the present study, we show that ethylcysteine enhances the NBT reduction by mouse peritoneal macrophages in vitro and...
ex vivo and enhances the luminol-dependent chemiluminescence in rat peritoneal macrophages and white blood cells ex vivo.

Materials and Methods

Animals: Male ICR mice (4 weeks of age; Charles River Japan, Ltd., Kanagawa, Japan) and male Wistar rats (250-300 g; Seiwa Experimental Animals, Ltd., Fukuoka, Japan) were used. Animals were housed at 23±2°C and 50±5% humidity, and they were allowed free access to food and water.

Drugs: L-Cysteine ethylester hydrochloride (Cystanin®, ethylcysteine; Yoshitomi Pharmaceutical Industries, Japan), L-cysteine (Sigma Chemical Co., St. Louis, U.S.A.), N-acetyl-L-cysteine (Sigma), sodium azide (Sigma), superoxide dismutase (SOD, 3000 U/mg from bovine blood; Sigma) and catalase (33300 U/mg from bovine liver, thymol-free; Sigma), luminol (Wako Pure Chemicals, Ltd., Osaka, Japan) and luminol-binding microspheres (Lumisphere, 2 μm in diameter, 2×10^9/ml; Toray Industries, Inc., Kamakura, Japan) were used as test drugs.

In the in vitro experiments, test drugs were dissolved in Hanks' balanced salt solution without phenol red (HBSS) at pH 7.4. In the in vivo and ex vivo experiments, test drugs were dissolved in 0.5% methylcellulose solution and sterile physiological saline for the oral and intraperitoneal treatment, respectively.

Stimulants: Zymosan A, concanavalin A (Con A), N-formyl-L-methionyl-L-leucyl-L-phenylalanine (FMLP) and phorbol-12-myristate acetate (PMA) were purchased from Sigma Chemical Co., and they were used as stimulants.

Preparation of opsonized zymosan (OZ): Zymosan A (7.5 mg) was boiled for 30 min and then centrifuged at 250×g for 10 min. This procedure was repeated three times in Dulbecco's phosphate-buffered saline (pH 7.4) to make the supernatant clear. The pelletted zymosan was suspended in 1 ml of fresh mouse or rat serum and incubated at 37°C for 30 min. After the incubation, OZ was washed three times and adjusted to the concentration of 1 mg/ml in HBSS.

Preparation of peritoneal macrophages in mice or rats: Peritoneal macrophages in mice and rats were obtained 3 days after the casein injection by the previously described method (7). The peritoneal exudate cells were obtained by washing the peritoneal cavity with 10 ml of HBSS containing 10 units/ml of heparin. When the cell types were determined morphologically by Giemsa staining, the peritoneal fluids were found to be composed of 70-80% macrophages and 10-20% lymphocytes. Viable cells were counted by the trypan blue exclusion test and adjusted to the concentration of 5×10^9/ml.

Preparation of white blood cells of rats: White blood cells were obtained from heparinized (10 units/ml) rat arterial bloods, and neutrophils were isolated by mono-poly resolving medium (Flow Laboratories, North Ryde, NSW, Australia). The cells were washed three times in HBSS by centrifugation at 4°C. The neutrophil purity was greater then 95%, and cell viability was more than 95%.

Preparation of peritoneal leukocytes in rats: Peritoneal polymorphonuclear leukocytes in rats were obtained 4 hr after the injection of 10 ml of 5% casein. Peritoneal exudate cells were found to be composed of more than 95% polymorphonuclear leukocytes.

NBT reduction of macrophages: The cell suspension (5×10^6/ml, 500 μl) was preincubated with or without test drugs at room temperature for 10 min. Then the reaction mixtures were incubated with 1 ml of 0.1% NBT solution and 10 μl of stimulants at 37°C for 30 min. NBT reduction of macrophages was measured under a microscope by the previously described methods (1). Results are expressed as % of cells that possess NBT-reducing activity.

Measurement of chemiluminescence: One-half milliliter of the cell suspension (5×10^6/ml, 500 μl) was preincubated with or without test drugs at room temperature for 10 min. Then the reaction mixtures were incubated with 1 ml of 0.1% NBT solution and 10 μl of stimulants at 37°C for 30 min. NBT reduction of macrophages was measured under a microscope by the previously described methods (1). Results are expressed as % of cells that possess NBT-reducing activity.

Measurement of chemiluminescence: One-half milliliter of the cell suspension (5×10^6–5×10^6) was preincubated with or without 10 μl of test solution at room temperature for 10 min. Then 10 μl each of prewarmed luminol (40 μg/ml) and OZ were added to the cell suspension. In other experiments, 15 μl of luminol (3×10^7) and 10 μl of rat serum were added to the leukocyte suspension. This mixture was mixed well and placed in the reaction chamber of a Chem-Glow photometer (Aminco, Silver Spring, U.S.A.) using the circulating system (NITI-ON Medical and Physical Instruments mfg, Co., Ltd., Chiba,
Japan) during the course of the reaction. The chemiluminescence was measured at 37°C. The results are expressed as the peak counts and/or the integrated counts of chemiluminescence.

**Statistical analysis:** Results are shown as the mean value or mean±S.D. The statistical analysis was performed using a one way layout.

**Results**

1. Effect on NBT reduction of macrophages ex vivo and in vitro

Ethylcysteine, at doses of 30 mg/kg (p.o. and i.p.), significantly enhanced the OZ-induced NBT reduction of mouse peritoneal macrophages (Table 1) and the number of cells having NBT reducing activity was significantly increased by the treatment with ethylcysteine at doses of 3 and 30 mg/kg (p.o.) and 30 mg/kg (i.p.). In the in vitro experiments, the OZ-induced NBT reduction of peritoneal macrophages stimulated by casein was enhanced by ethylcysteine at 30 μM (Table 2). ConA (200 μg/ml), FMLP (10 μM) and PMA (30 nM) enhanced the OZ-induced NBT reduction of macrophages. The enhancement of OZ-induced NBT reduction by Con A, FMLP or PMA was diminished by the addition of SOD (30 μg/ml), sodium azide (10 μM) or catalase (200 μg/ml). This enhancement was completely diminished by the addition of three agents. Ethylcysteine (30 μM) significantly accelerated the en-

| Drug          | Dose (mg/kg) | Ratio (%) | Cell number (10⁶) |
|---------------|--------------|-----------|------------------|
| Control       | 0            | 4.1±1.2   | 2.8±1.2          |
| Ethylcysteine | 3            | 6.3±1.9   | 7.1±4.8*         |
|               | 30           | 8.4±2.6*  | 7.2±1.9*         |
| Control       | 0 (i.p.)     | 5.2±1.9   | 5.1±3.3          |
| Ethylcysteine | 30 (i.p.)    | 14.6±3.3**| 15.8±2.7**       |

ICR mice were injected i.p. with 2 ml of 5% casein suspension (on day 0). Ethylcysteine was administered on days 0, 1 and 2. The peritoneal macrophages were collected on day 3. The cell suspension was incubated with NBT solution and opsonized zymosan (OZ) at 37°C for 30 min. Results are shown as the mean±S.D. (N=5). *P<0.05, **P<0.01, significantly different from the control group.

| Drug          | Conc (μM) | +None | +Con A | +FMLP | +PMA |
|---------------|----------|-------|--------|-------|------|
| Control       | 0        | 3.5±0.9 | 13.0±1.1 | 10.2±1.8 | 18.8±2.0 |
| Ethylcysteine | 3        | 5.0±0.4 | 15.8±1.8 | 13.8±0.9 | 20.4±2.6 |
| (E)           | 30       | 8.6±2.2**  | 20.8±0.6** | 16.4±1.3** | 26.9±2.8** |
| SOD (S)       | 30*a     | 2.9±1.2 | 4.7±0.7** | 5.6±0.7** | 9.7±0.6** |
| Sodium azide (SA) | 10   | 1.7±0.2**  | 3.1±0.7** | 2.9±0.2** | 3.6±0.7** |
| Catalase (C)  | 200*a    | 2.4±0.4 | 3.9±1.1** | 3.4±0.4** | 5.6±0.4** |
| S+SA+C        | 2.2±0.4** | 0.9±0.1 | 1.1±0.1** | 0.7±0.1** | 3.3±0.9** |
| Ethylcysteine + S+SA+C | 2.7±0.7 | 2.1±0.9** | 1.8±0.2** | 3.3±0.9** |

*a μg/ml, b 30 μM. The peritoneal macrophages were preincubated with test compounds at room temperature for 10 min. After the addition of 0.1% NBT solution and OZ (1 mg/ml), these macrophages were incubated with or without Con A (200 μg/ml), FMLP (10 μM) or PMA (30 nM) at 37°C for 30 min. Results are shown as the mean±S.D. (N=4–8). **P<0.01, significantly different from the control group.
enhancement of the OZ-induced NBT reduction of macrophages by the addition of Con A, FMLP or PMA. This enhancing effect of ethylcysteine was diminished by the addition of SOD, sodium azide and catalase.

2. Effects on chemiluminescence generated from rat peritoneal macrophages and white blood cells

1) Influence of macrophage number and OZ concentration: The peak time of chemiluminescence of peritoneal macrophages was 20–40 sec after the addition of OZ and luminol. The increment of the peak count of this chemiluminescence was proportional to that of OZ concentrations (25–100 µg) (Fig. 1) and cell number (5 x 10^4–5 x 10^6) (Fig. 2). The maximum peak count was obtained under the experimental condition using 5 x 10^6 cells and 100 µg of OZ (Fig. 3). The integrated counts for the incubation of 2–5 min were nearly proportional to the maximum peak count (Fig. 4). Therefore, the effects of test drugs were studied on the chemiluminescence during the incubation of cells with test drugs and stimulants for 3 min.

2) Effect of ethylcysteine in vitro: Ethylcysteine did not increase the peak count and integrated counts of the OZ-induced chemiluminescence of macrophages at concentrations of 100 µM (Table 3). At 300 µM, this drug significantly decreased both the peak
count and integrated counts of chemiluminescence. The OZ-induced chemiluminescence was decreased by N-acetyl-L-cysteine at 300 μM, but not by L-cysteine. SOD, sodium azide and catalase significantly decreased the peak count and integrated counts of the chemiluminescence at 30 μg/ml, 3-10 μM and 200 μg/ml, respectively; and the combination of SOD, sodium azide and catalase completely diminished the OZ-induced chemiluminescence. As these drugs decreased both the peak count and integrated counts of the chemiluminescence response to the same degree, the effects of these drugs on the chemiluminescence response were mainly carried out using the peak count as a marker of the chemiluminescence.

3) Effect of ethylcysteine ex vivo: Ethylcysteine significantly increased the macrophage number in the peritoneal cavity of rats at doses of 10 and 3–10×3 mg/kg (i.p.) (Table 4). The OZ-induced chemiluminescence of peritoneal macrophages was significantly enhanced by the treatment with this drug both at the above doses and at 3–30×3 mg/kg (p.o.). L-cysteine did not affect the OZ-induced chemiluminescence at 30 mg/kg (i.p.). N-Acetyl-L-cysteine increased the OZ-induced chemiluminescence at 30 mg/kg (i.p.), but not significantly. In addition, the chemiluminescence of white blood cells was enhanced by the treatment with ethylcysteine at doses of 10 (i.p.), 3–10×3 (i.p.), 30 (p.o.) and 30×3 mg/kg (p.o.) (Table 5). The OZ-induced chemiluminescence of peritoneal leukocytes was not enhanced by the treatment with ethyl-cysteine at doses of 3–30 mg/kg (i.p.), but the lumisphere-induced chemiluminescence of peritoneal leukocytes was significantly enhanced at 30 mg/kg (i.p.) (Table 6).
### Table 3. Effect of ethylcysteine on the chemiluminescence of rat peritoneal macrophages in vitro

| Drug                  | Concen (μM) | Chemiluminescence | Peak count $10^3$ cpm | Integrated counts $10^3$ |
|-----------------------|-------------|-------------------|------------------------|--------------------------|
| Control               | 0           |                   | 85±21                  | 308±50                   |
| Ethylcysteine         | 100         |                   | 80±9                   | 332±26                   |
| Control               | 0           |                   | 89±15                  | 266±27                   |
| Ethylcysteine         | 300         |                   | 56±12**                | 178±22**                |
| Control               | 0           |                   | 51±8                   | 244±5                    |
| L-Cysteine            | 300         |                   | 45±3                   | 201±42                   |
| N-Acetyl-L-cysteine   | 300         |                   | 38±7*                  | 164±15*                 |
| Control               | 0           |                   | 89±15                  | 232±32                   |
| SOD (S)               | 3a          |                   | 93±17                  | 248±74                   |
| Sodium azide (SA)     | 3           |                   | 48±16**                | 116±38**                |
|                       | 10          |                   | 32±12**                | 54±22**                 |
| Control               | 0           |                   | 21±7**                 | 30±18**                 |
| Catalase (C)          | 200a        |                   | 45±12**                | 137±18**                |
| Control               | 0           |                   | 97±18                  | 254±42                   |
| Sb+SAc+C              |             |                   | 5±1**                  | 12±4**                  |

a: μg/ml, b: 30 μM, c: 3 μM. The peritoneal macrophages were preincubated with test compounds at room temperature for 10 min. After the addition of OZ and luminol, the chemiluminescence of macrophages was measured at 37°C for 3 min. Results are shown as the mean±S.D. (N=3–8). *P<0.05, **P<0.01, significantly different from the control group.

### Table 4. Effect of ethylcysteine on the chemiluminescence of rat peritoneal macrophages ex vivo

| Drug                  | Administration route | Dose (mg/kg) | Cell number $10^b$ | Peak count of CL $10^3$ cpm |
|-----------------------|----------------------|--------------|--------------------|-----------------------------|
| [Single administration] |                       |              |                    |                             |
| Control               | i.p.                 | 0            | 94±20              | 60±25                       |
| Ethylcysteine         | i.p.                 | 3            | 111±49             | 82±10                       |
|                       | i.p.                 | 10           | 148±45**           | 95±11*                      |
| Control               | i.p.                 | 0            | 153±68             | 53±8                        |
| L-Cysteine            | i.p.                 | 30           | 121±6              | 54±16                       |
| N-Acetyl-L-cysteine   | i.p.                 | 30           | 96±22              | 74±12                       |
| Control               | p.o.                 | 0            | 94±36              | 48±21                       |
| Ethylcysteine         | p.o.                 | 3            | 103±10             | 30±9                        |
|                       | p.o.                 | 30           | 129±33             | 38±25                       |
| [Repeated administration] |                       |              |                    |                             |
| Control               | i.p.                 | 0            | 146±42             | 76±34                       |
| Ethylcysteine         | i.p.                 | 3            | 347±103**          | 203±28*                     |
|                       | i.p.                 | 10           | 375±35**           | 194±95*                     |
| Control               | p.o.                 | 0            | 94±36              | 48±21                       |
| Ethylcysteine         | p.o.                 | 3            | 88±27              | 67±16*                      |
|                       | p.o.                 | 30           | 105±32             | 66±18*                      |

SD rats were injected i.p. with 20 ml of 5% casein suspension (on day 0). Test compounds were administered on day 2 or on days 0–2. The peritoneal macrophages were collected on day 3. The OZ-induced chemiluminescence of macrophages was measured at 37°C for 3 min. Results are shown as the mean±S.D. (N=4–8). *P<0.05, **P<0.01, significantly different from the control group.
Table 5. Effect of ethylcysteine on the chemiluminescence of rat white blood cells ex vivo

| Drug       | Administration route | Dose (mg/kg) | Peak count $10^6$ | % of control |
|------------|----------------------|--------------|-------------------|--------------|
| Control    | i.p.                 | 0            | 52±49             | 100          |
| Ethylcysteine | i.p.                 | 3            | 88±14             | 169          |
| Control    | p.o.                 | 0            | 35±16             | 100          |
| Ethylcysteine | p.o.                 | 3            | 53±12             | 151          |
| Control    | p.o.                 | 30           | 87±13             | 249          |

[Single administration]

| Drug       | Administration route | Dose (mg/kg) | Peak count $10^6$ | % of control |
|------------|----------------------|--------------|-------------------|--------------|
| Control    | i.p.                 | 0            | 52±28             | 100          |
| Ethylcysteine | i.p.                 | 3            | 155±87*           | 298          |
| Control    | p.o.                 | 0            | 35±16             | 100          |
| Ethylcysteine | p.o.                 | 3            | 77±46             | 220          |
| Control    | p.o.                 | 30           | 125±23*           | 357          |

[Repeated administration]

Experimental conditions are shown in Table 4. Results are shown as the mean±S.D. (N=4–5). *P<0.05. **P<0.01, significantly different from the control group.

Table 6. Effect of ethylcysteine on the chemiluminescence of rat peritoneal leukocytes ex vivo

| Drug       | Dose (mg/kg) | Opsonized zymosan | Lumispherine |
|------------|--------------|--------------------|--------------|
| Control    | 0            | 133±18             | 4.6±1.7      |
| Ethylcysteine | 3          | 127±43             | 6.0±2.3      |
|            | 30           | 137±12             | 11.0±5.1**   |

Test compounds were administered into SD rats immediately before the intraperitoneal injection of 5 ml of 5% casein suspension. The peritoneal leukocytes were collected 4 hr after the casein injection. The chemiluminescence was measured at 37°C for 3 min. Results are shown as the mean±S.D. (N=4–8). **P<0.01, significantly different from the control group.

Discussion

The actual killing and digestion of microorganisms by phagocytic cells are accomplished through the action of both myeloperoxidase and the active oxygens provided by the respiratory burst (2, 9, 10). The measurement of intracellular NBT reduction under the microscope is useful since it reveals the generation of intracellular active oxygens following activation of membrane-associated metabolism during phagocytosis of OZ by phagocytic cells (11). In this study, the present data indicated that ethylcysteine augmented the OZ-induced NBT reduction of macrophages ex vivo.

The stimulation of the plasma membranes by Con A (12, 13), PMA (14) and FMLP (15, 16) can produce a large amount of superoxide and hydrogen peroxide in phagocytic cells. It is clear that the above stimulants enhance the NBT reduction of macrophages to OZ, and the accelerating effect of these stimulants is diminished by the addition of SOD, which converts superoxide to H₂O₂ (17), sodium azide [myeloperoxidase inhibitor (18) and O₂ quencher (19)], or catalase (H₂O₂ inhibitor) (20). The potentiating effects of Con A, FMLP or PMA on the OZ-induced NBT reduction of macrophages were accelerated by the treatment with ethylcysteine. The accelerating effects of
ethylcysteine are diminished by the addition of SOD, sodium azide and catalase. In this experiment, because washed OZ was used as a stimulant, the direct effect of the third component of complement, C3, was suggested to be negligible. These results suggest that the potentiating effect of ethylcysteine on NBT reduction of macrophages might be attributed to the enhancement of both the myeloperoxidase activity and the generation of intracellular reactive oxygen radicals. In order to confirm the potentiating effect of ethylcysteine on the generation of reactive oxygen radicals, the effect of this drug on chemiluminescence of leukocytes or macrophages was examined.

In in vitro experiments, the OZ-induced chemiluminescence of macrophages is not enhanced but rather inhibited by the treatment with a high concentration of ethylcysteine (300 μM). Since the OZ-induced chemiluminescence has been reflected to intra- and extra-cellular events of phagocytic cells (21), the effect of ethylcysteine on the chemiluminescence may be inconsistent with those on NBT reduction. N-Acetyl-L-cysteine weakly inhibits the OZ-induced chemiluminescence of peritoneal macrophages at 300 μM, but L-cysteine does not inhibit the chemiluminescence. It may be possible that these drugs inhibit the chemiluminescence at a higher concentration. Recently, N-acetylcysteine at a concentration of 3 mM or higher was reported to inhibit the OZ-induced chemiluminescence of human neutrophils (22). Cysteine (300 μM) can inhibit the enhancement of the chemiluminescence of OZ, PMA or FMLP-stimulated human neutrophils (22, 23), but enhanced the activity of the hexose monophosphate shunt of OZ or PMA-stimulated human neutrophils (24). These findings show that cysteine and cysteine derivatives selectively neutralize the reactivity of harmful reactive oxidants released by phagocytic cells, while the intracellular generation of antimicrobial oxidants remains intact (22, 23). It seems that ethylcysteine as well as cysteine or N-acetyl-L-cysteine can neutralize the extracellular reactive oxidants released by phagocytic cells.

The OZ-induced chemiluminescence of rat peritoneal resident macrophages is enhanced by the oral and intraperitoneal treatment with ethylcysteine at the same doses as shown in the acceleration of the decrease of viable E. coli in the blood and liver of mice (7), and this enhancing effect of ethylcysteine is shown on the chemiluminescence of the white blood cells of rats. On the other hand, this drug enhances the lumisphere-induced chemiluminescence of leukocytes, but not the OZ-induced chemiluminescence. The lumisphere-induced chemiluminescence of human polymorphonuclear leukocytes has been reported to be mainly due to intracellular reactive oxygen radicals (25, 26). Because this chemiluminescence directly reflects the generation of highly reactive oxygen in the phagosomes, measurement of the lumisphere-induced chemiluminescence may be more suitable as an indicator of intracellular microbicidal activity (26). From these findings, ethylcysteine may enhance the intracellular generation of microbicidal oxidants in macrophages and leukocytes. MDP and its analogs have been shown to enhance the OZ-induced chemiluminescence of leukocytes ex vivo (27), and these effects may be attributed to the nonspecific host resistance to infection by microorganisms such as E. coli (28) and Ps. aeruginosa (29). Therefore, this suggests that ethylcysteine is able to enhance the intracellular generation of microbicidal oxidants in phagocytic cells and to enhance the nonspecific host resistance to infection. The chemiluminescence to other amplifiers such as lucigenin (30, 31) may be necessary to study the effect of drugs on the production of active oxygen species and the myeloperoxidase-H2O2-halide system in phagocytic cells.

In conclusion, ethylcysteine enhanced the OZ-induced NBT reduction of macrophages in mice and accelerated the enhancement of NBT reduction by the addition of Con A, FMLP or PMA; and this drug enhanced the OZ-induced chemiluminescence of rat peritoneal macrophages and white blood cells ex vivo. In addition, this drug enhanced the lumisphere-induced chemiluminescence of rat peritoneal leukocytes ex vivo. These results suggest that ethylcysteine may enhance the intracellular generation of microbicidal oxidants in phagocytic cells.
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