

**Evaluation of the Effects of Modified Arabinoxylan
from Rice Bran (BioBran/MGN-3)
in Preventing Asthma and Relieving Symptoms
in a Mouse Model of Asthma**

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Objective

The effects of BioBran/MGN-3 in preventing asthma and relieving symptoms was studied in a mouse model of asthma induced with toluene diisocyanate (TDI).

Experimental method

1. Mouse model of asthma

Female BALB/c mice received 1 mL of a 10% TDI/ethyl acetate solution intranasally daily for 7 days to produce antigen sensitisation. Three weeks later, the same solution was administered similarly twice weekly and a total of 24 challenges performed over a period of 12 weeks. Changes in the levels of IgG1 and IgE type antibodies against TDI, thickening of the mucous membrane, and level of nasal secretions were assessed. This experimental model, which has been developed in our laboratory, has greater similari-

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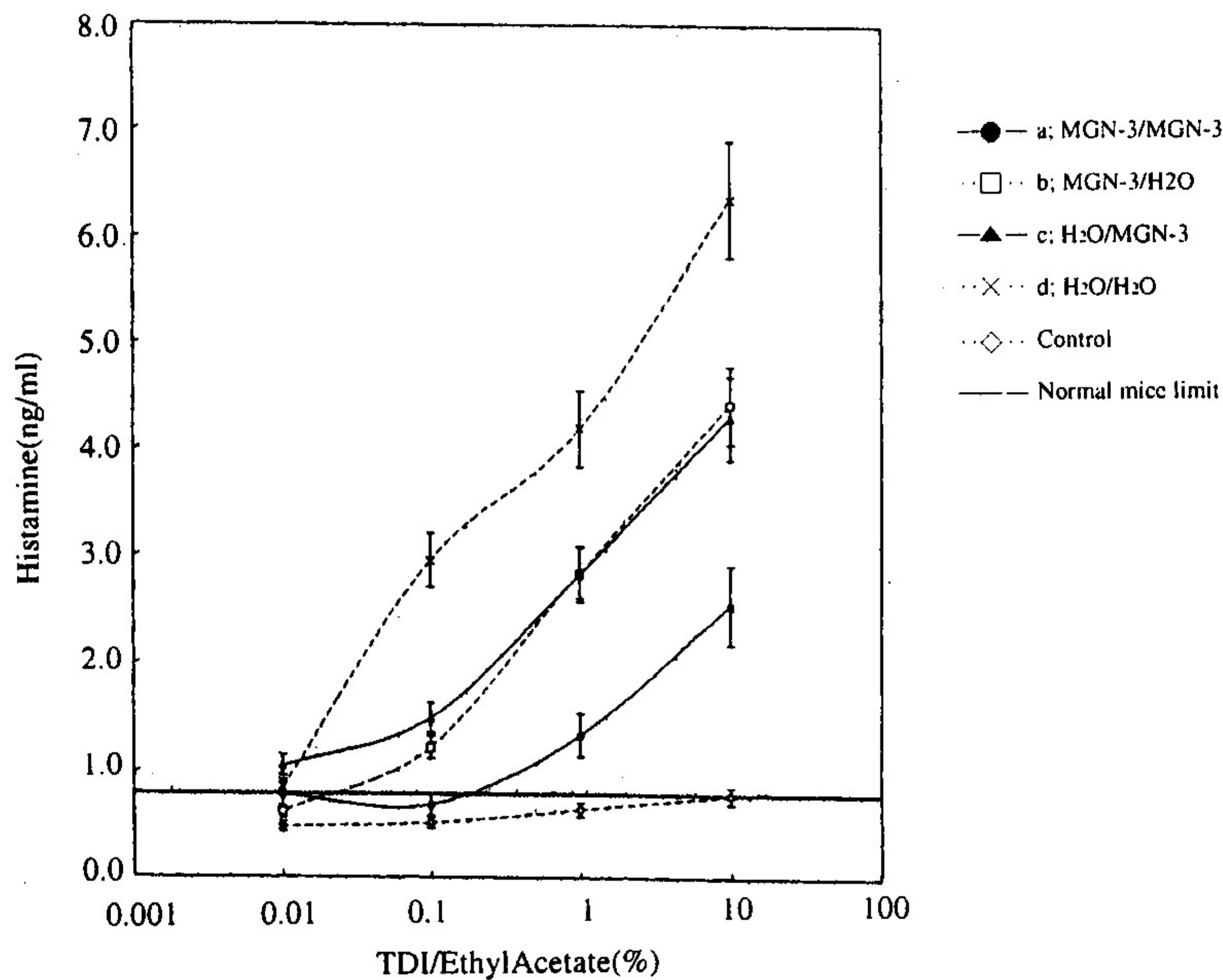


Fig.1 Serum level of histamine after challenge with various concentration of TDI

ties to human asthma than others producing short-term antigen sensitisation.

2. Administration

BioBran/MGN-3 (Daiwa Pharmaceutical Co., Ltd.) was dissolved at 2 g/L in drinking water and mice allowed to drink it *ad libitum*.

3. Experimental groups

- a: One group of mice received one month of pretreatment, TDI sensitisation and challenge (the MGN-3/MGN-3 group).
- b: A second group received one month of pretreatment and TDI sensitisation (the MGN-3/H2O group).
- c: A third group received only the challenge with TDI (the H2O/MGN-3 group).
- d: A fourth group of mice received no treatment (the H2O/H2O group).

4. Evaluation

Blood histamine concentration, eosinophil count in bronchoalveolar lavage fluid (BALF), TDI ear lobe application test, and serum levels of IgG1, IgG2a, and IgE antibodies against TDI during the challenges were measured.

5. Statistical analysis

ANOVA was used.

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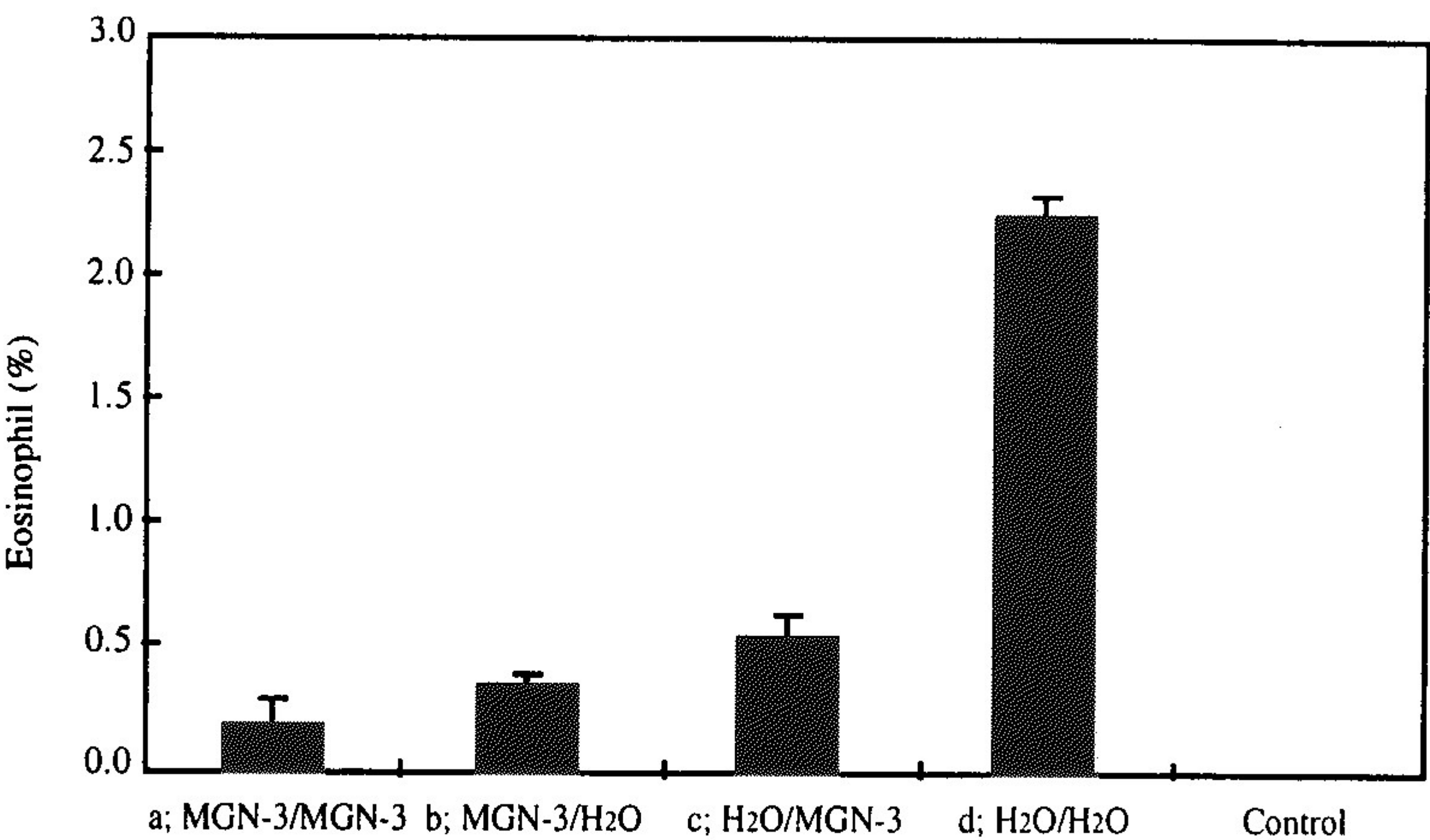


Fig.2 Percentage of eosiophils in BALF from TDI mice

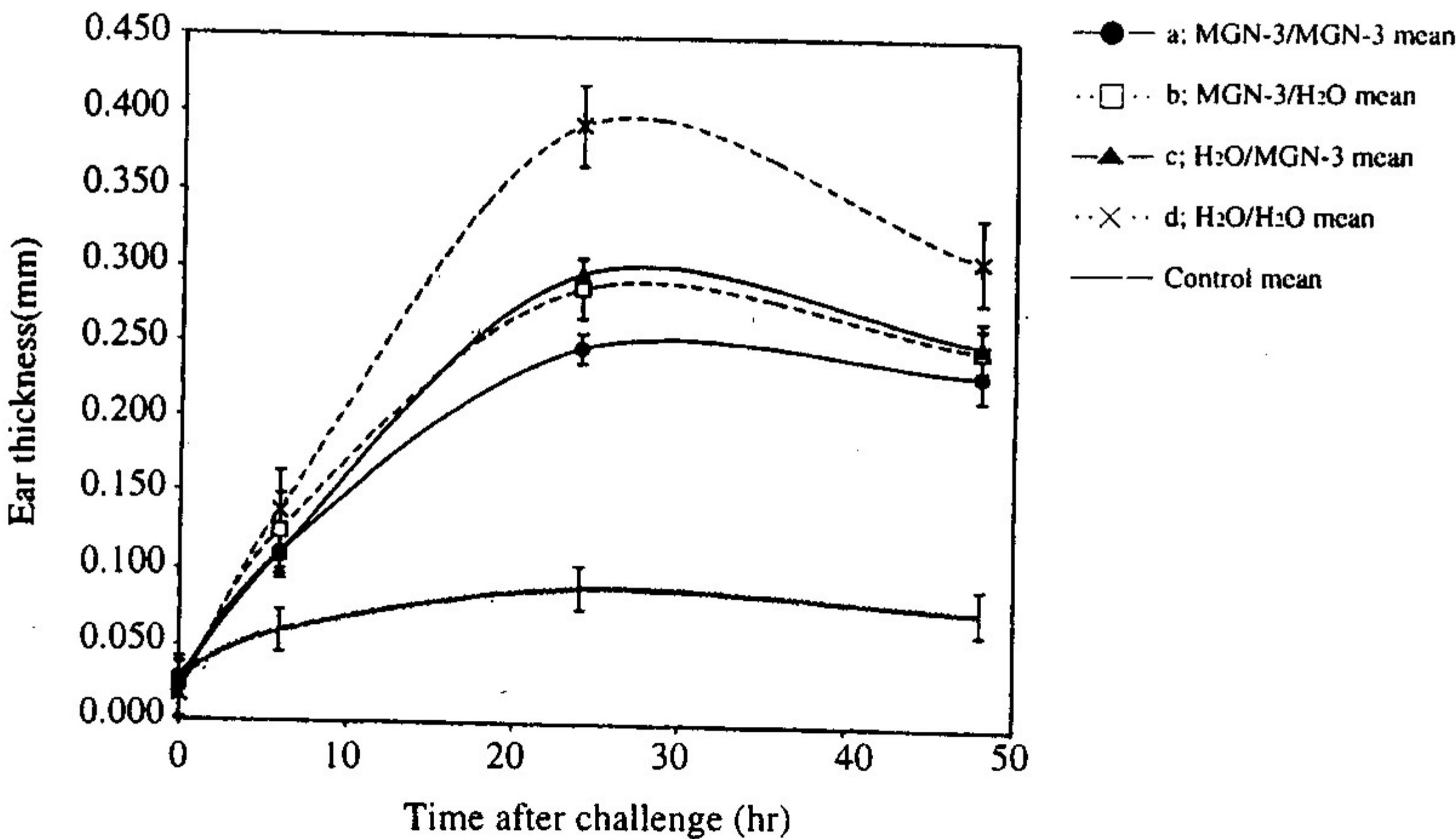


Fig.3 Ear thickness* of mice after TDI challenge

* Ear thickness = right ear (TDI challenge) --left ear (vihecle)

Results

The peak blood concentration of histamine 7 minutes after challenge with 10% TDI was 2.5 ± 0.53 , 4.2 ± 0.75 , 4.3 ± 0.78 , and 6.4 ± 0.87 mg/mL for the MGN-3/MGN-3, MGN-3/H₂O, H₂O/MGN-3, and H₂O/H₂O groups, respectively. Groups treated with MGN-3 had significantly lower values than those that were nontreated. In challenge experiments using 0.01%, 0.1%, 1%, and 10% TDI solutions, the sensitivity of the MGN-3 treatment groups was 10-100 times lower than in the nontreated groups (Fig.1). The

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eosinophil counts in BALF were 5-10 times lower in the MGN-3 treatment groups than in the nontreatment group (**Fig.2**) and ear lobe thickness was significantly less in the MGN-3 treatment groups following TDI application (**Fig.3**).

Conclusion

BioBran/MGN-3 produced clear effects in preventing asthma and relieving symptoms in this mouse model of asthma induced with TDI. BioBran/MGN-3 had no effect on the production of IgG1 and IgE antibodies induced through Th2 cells, suggesting an inhibitory action on mast cells.