Acute and Repeated Inhalation Toxicity of 1-Bromopropane in SD Rats

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Abstract: Acute and Repeated Inhalation Toxicity of 1-Bromopropane in SD Rats: Hyeon-Yeong Kim *et al.* Industrial Chemicals Research Center, Industrial Health Research Institute, Korea—The acute and repeated inhalation toxicity of 1-bromopropane (1-BP) in SD rats were investigated. LC₅₀ for four-hour exposure was 14,374 ppm (95% confidence limit: 13,624–15,596 ppm). It was revealed to be irritating to the eyes with lacrimation in all four-hour exposure rats. No other abnormal clinical signs and gross findings related to the 1-BP exposure were observed. An experiment on repeated exposure to 0, 50, 300, and 1,800 ppm for six hrs/day, five days/week, for eight weeks was conducted. A decrease in body weights and increase in relative liver weight in both male and female rats were observed in the 1,800 ppm exposure group ($p < 0.001$ vs. control group). No other significant changes in feed consumption, urinalysis, hematology and serum biochemistry were observed. Histopathological examinations did not reveal any 1-BP-related changes.

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Key words: 1-Bromopropane, Inhalation Toxicity, LC₅₀

It is difficult to choose appropriate cleaning solvents for industrial use for many reasons such as toxicity and environmental unfriendliness. Up to now, halons have been used as cleaning solvents in the chemical and electronic industries. But they are now being replaced by alternatives because of their ozone-depleting and global warming characteristics¹⁾. In Korea, 2-bromopropane (2-BP) has been used in the place of halons, but 2-BP was found to cause reproductive and

hematopoietic disorders in local workers exposed to solvents containing 2-BP²⁻⁶⁾, which caused the Korean Ministry of Labor to establish the threshold limit value (TLV) for 2-BP in the workplace as 1 ppm⁷⁾. Owing to the toxicity of 2-BP, there has been a growing tendency to use 1-bromopropane (1-BP) as an alternative cleaning solvent to 2-BP. Even though there are no exact data on the total production of 1-BP, more than 100,000 tons of bromo compounds would have been produced annually in the U.S. alone⁸⁾.

There are very few data available on the toxicity of 1-BP and its established TLV in the workplace. LC₅₀ for thirty-minute exposure was 253 g/kg in rats⁹⁾. Intraperitoneal LD₅₀ of 1-BP was reported to be 2.5 g/kg in mice and 2.9 g/kg in rats¹⁰⁾. 1-BP has a depressing action on the central nervous system (CNS)¹¹⁾ and is reported to be irritating to the skin and eyes of mice⁹⁾. Exposure of animals to the anesthetic concentration may result in injury to the lungs and liver¹¹⁾. Takeuchi *et al.*¹²⁾ observed that the inhalation exposure of 1-BP at 1,000 ppm, eight-hours/day for 4 weeks, decreased the conduction velocity of the peripheral nerves in rats. They also observed peripheral nerve and CNS disorders in rats exposed to the same concentration for 5 to 6 weeks.

But the above inhalation toxicity of 1-BP was not confirmed by other investigators. This study was carried out to assess the acute and repeated inhalation toxicity of 1-BP.

Materials and Methods

Chemicals: Chemicals used in this study were of reagent grade and purchased from commercial sources. 1-BP (Lot No. 7B2212) was obtained from Junsei Chemical Co., Ltd. (Tokyo, Japan).

Animals: Ten-week-old Sprague-Dawley (SD) rats (SPF grade) of both sexes were purchased from Dae Han Laboratory Animal Research center Co., Ltd. (Eumseong,

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Korea). After one week of acclimation, 25 males (233.7 ± 32.1 g) and 25 females (186.3 ± 6.9 g) were chosen for the acute inhalation toxicity test, and 40 males (267.2 ± 6.2 g) and 40 females (199.3 ± 3.8 g) were used for the repeated inhalation toxicity test. The rats were housed individually in wire-bottomed 5-straight stainless-steel cages placed in exposure chambers. The cages were maintained at $23 \pm 2^\circ\text{C}$, 40–70% humidity, 12-h light/12-h dark cycle (light during 09:00–21:00), 11–15 times ventilation/h, and 5–15 mmAq negative pressure. The rats were fed with the sterilized pellets (Jeil Feed Co., Ltd., Taejon, Korea) and sterilized tap water *ad libitum* through both the acclimation and observation periods.

Condition of chambers: Temperature, relative humidity, pressure and air ventilation were recorded by the environmental controller (Model No. ICS-20RG, Shibata Co., Ltd., Japan). Calibration of the concentration of 1-BP in the chambers was carried out with a standard Chemicals (Lot No. 7B2212, Junsei Chem. Co., Ltd., Japan), air pump (Model APN-110KV-1, Iwaki Co., Ltd., Japan), gas meter (Model DC-2A, Shinagawa Co., Ltd., Japan) and Teflon® bags. The detection conditions for gas chromatography (GC) (Model GCS-14PFFS, Shimadzu, Japan) for 1-BP were as follows: detector, FID; column, silicon DC-200 15% Chromosorb with mesh of 80/100 and 0.5 m length; detector temperature, 150°C ; oven temperature, 100°C ; injector temperature, 150°C ; injection volume, 1 ml of gas sample. The concentration of 1-BP in the chambers during the exposure was recorded with the GC every 15 min.

Animal experimentation: Whole-body exposure chambers (Model No. SIS-20RG, Shibata Co., Ltd., Japan) including a gas generator (Model No. VG-4R, Shibata Co., Ltd., Japan) were used for exposure of the rats to 1-BP. For the acute inhalation toxicity test, 25 male and 25 female rats were entered. Animals of each sex were divided into five groups (0, 11,000, 13,000, 15,000 and 17,000 ppm). The rats were observed for two weeks after exposure, focusing on clinical appearances and death. The health status of the rats was observed daily for 14 days. At the end of the observation period, all the rats were sacrificed by CO_2 gas anesthesia. Abnormal tissues were grossly taken and fixed in 10% neutral buffered formalin. These were embedded in paraffin, sectioned, and stained with hematoxylin-eosin. LC_{50} was determined by the Lithfiled-Wilcoxon method⁽¹³⁾.

As a repeated inhalation experiment, a group of 10 male and female rats were exposed to 0 (control), 50, 300 and 1,800 ppm for six hrs a day, five days a week, for eight weeks. All the rats were inspected daily for clinical signs. Body weight and feed consumption were measured twice a week during the inhalation period. Urine samples were collected 24 h before the end of the experiment, and analyzed for red blood cells, white blood

cells, bilirubin, urobilinogen, ketones, protein, nitrite, glucose, pH, specific gravity and with a test strip (Bio-Gen 10SGLM, Yeongdong Pharm Co., Ltd., Seoul, Korea). All the rats were anesthetized with dry ice (CO_2), and bled for hematology and biochemistry from the posterior vena cava. In hematological examinations, white blood cell, red blood cell, hemoglobin, hematocrit, mean corpuscular volume, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration, red cell volume distribution width, platelet count and mean platelet volume were determined with a hematological auto analyzer (Sysmex F-820, Japan). The differential leucocyte count was determined on the blood smears. In serum biochemical examinations, aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase, glucose, blood urea nitrogen, protein, cholesterol, creatinine, sodium and total bilirubin were determined with a biochemical analyzer (TBA20FR, Japan). Organ weights were measured for the thymus, adrenal, testis, heart, lung, kidney, spleen, liver and brain. These tissues were taken and fixed in 10% neutral buffered formalin. The tissues were processed for standard paraffin embedding prior to sectioning at $5 \mu\text{m}$ and stained with hematoxylin-Eosin and/or PAS-hematoxylin.

Statistical analysis: Two-way analysis of variance (ANOVA) and Duncan's multiple test were adopted for statistical testing.

Results

Acute inhalation toxicity test

Environmental and concentration monitoring: All the rats were housed at a temperature of $22.5\text{--}23.3^\circ\text{C}$, a relative humidity of 43.8–65.3%, a pressure of $-9.2\text{--}-10.2$ mmAq, and air ventilation of $196.7\text{--}201.0$ l/min (12/h). These parameters were within the established value $\pm 4\%$ (Table 1).

Clinical findings: All treated groups were observed to have piloerection, decreased activity, ataxia and lacrimation within 1 h after exposure to 1-BP. As time went by, they did not respond to a noise level of about 100 phones. All male rats in the 11,000 ppm group and 13,000 ppm group survived the experiment, but two male rats in the 15,000 ppm group were dead within 6 h. The same results were observed in female rats in the 11,000 ppm group, but one female rat in the 13,000 ppm group was dead within 12 h. Four female rats in the 15,000 ppm group were dead within 24 h. All surviving rats recovered to the normal condition after 24 h.

Necropsy findings: There were no gross pathological findings in any of the animals in the experiment.

Histopathological findings: Some treated rats showed cytoplasmic vacuolation in the hepatocytes around the central veins, but without dose-dependency. No other specific histopathological findings were observed in the

Table 1. Concentration of 1-BP during exposure in acute inhalation toxicity study

Groups	Concentration (ppm)			
	Establishment	Upper	Lower	Mean $\pm$ SD
Group 1	11,000	11,147.5	10,392.5	10,909.4 $\pm$ 185.99
Group 2	13,000	13,221.2	12,855.5	13,013.2 $\pm$ 104.23
Group 3	15,000	15,565.7	14,498.3	15,129.3 $\pm$ 383.92
Group 4	17,000	17,704.9	16,297.2	17,086.1 $\pm$ 587.08

Table 2. Effects of concentration of 1-BP on mortality in SD rats

Exposure Groups	Concentration (Mean $\pm$ SD)	No. of rats		No. of deaths			Total Mortality (%)
		male	female	male	female	Total	
Control	—	5	5	0	0	0	0
Group 1	10,909.4 $\pm$ 185.99	5	5	0	0	0	0
Group 2	13,013.2 $\pm$ 104.23	5	5	0	1	(1)	10
Group 3	15,129.3 $\pm$ 383.92	5	5	2	4	(6)	60
Group 4	17,086.1 $\pm$ 587.08	5	5	5	5	(10)	100

Table 3. Environmental conditions in the inhalation chamber during repeated exposure

Items	Chamber 0 (Control)	Chamber 1 (50 ppm)	Chamber 2 (300 ppm)	Chamber 3 (1,800 ppm)
T ($^{\circ}$ C)	22.9 $\pm$ 1.23	22.5 $\pm$ 1.21	22.8 $\pm$ 1.32	23.3 $\pm$ 1.28
RH (%)	45.5 $\pm$ 6.46	44.8 $\pm$ 6.52	44.8 $\pm$ 6.13	50.2 $\pm$ 1.80
P (mmH ₂ O)	−9.2 $\pm$ 0.22	−9.9 $\pm$ 0.21	−9.7 $\pm$ 0.34	302.6 $\pm$ 10.10
R (L/min)	199.7 $\pm$ 1.17	201.0 $\pm$ 1.17	196.7 $\pm$ 1.33	1,803.4 $\pm$ 39.84

T: Temperature, RH: Relative Humidity, P: Pressure, R: Flow Rate. All data values are expressed as the total mean (for 8 weeks) $\pm$ SD.

treated groups when compared with the control group.

Median lethal concentration (LC_{50}): LC_{50} (4 h) of 1-BP was 14,374 ppm (95% confidence limit: 13,624–15,596 ppm). The lowest lethal concentration ($LCLo$) was lower than 11,833 ppm (95% confidence limit: 7,829–13,033 ppm) and the concentration 100 percent kill (LC_{100}) was higher than 18,186 ppm (95% confidence limit: 16,616–26,632 ppm) (Table 2).

Repeated inhalation toxicity test

Environmental monitoring in chambers: Temperature, relative humidity, pressure, air ventilation and illumination cycle in the inhalation chambers were measured under the OECD guidelines for environmental control and are shown in Table 3. These parameters were within the established value of 4% (Table 4).

Clinical findings: 1,800 ppm treated groups were observed to show decreased activity and mild ataxia after

1 h exposure to 1-BP, but they recovered within 1 h after termination daily inhalation test.

Body weights: Changes in body weight during the whole inhalation period are shown in Fig. 1 (for males) and in Fig. 2 (for females). There was a statistically significant decrease in body weight in male rats from 5 weeks (39 days) inhalation of 1-BP ($p < 0.05$), and in female rats from 4 weeks (27 days) inhalation of 1-BP ($0.01 < p < 0.05$).

Feed consumption: There were no statistically significant changes between the control group and the treated groups in feed consumption (data not shown).

Urinalysis: The level of urobilinogen was decreased in male rats in the 1,800 ppm group ($p < 0.05$), but increased in female rats in the 300 ppm group and the 1,800 ppm group ($p < 0.001$). The level of bilirubin was increased in female rats in the 1,800 ppm group ($p < 0.001$). There were statistically significant increases in ketone

Table 4. Concentration of 1-BP during exposure in repeated inhalation toxicity study

Groups	Concentration (ppm)			
	Establishment	Upper	Lower	Mean $\pm$ SD
Group 1	—	0	0	0.0 $\pm$ 0.00
Group 2	50	52.7	46.6	50.2 $\pm$ 1.80
Group 3	300	320.2	286.7	302.6 $\pm$ 10.10
Group 4	1,800	1,852.5	1,756.9	1,803.4 $\pm$ 39.84

Fig. 1. Change in body weights of male SD rats that inhaled 1-bromopropane during the experiment. **Fig. 2.** Change in body weights of female SD rats that inhaled 1-bromopropane during the experiment.

bodies in both sexes in the 1,800 ppm group ($p < 0.05$) and in females in the 300 ppm group ($p < 0.05$). The level of leucocytes was increased significantly in females in the 1,800 ppm group ($p < 0.05$).

Necropsy findings: There were no gross pathological findings in any of the animals.

Organ weights: The relative organ weights (organ weight/100 g body weight) are summarized in Table 5 for the males and Table 6 for the females. The weights of liver and brain in male rats were increased dose-dependently. The weights of testis were increased in the 1,800 ppm group ($p < 0.01$). The weights of liver, kidney and ovary in female rats were significantly increased in the 1,800 ppm group, at the level of $p < 0.001$, $p < 0.01$, and $p < 0.01$, respectively.

Hematology: Table 7 shows that the white blood cell

count ($p < 0.01$), red blood cell count ($p < 0.01$), hematocrit ($p < 0.01$) and mean corpuscular volume ($p < 0.05$) significantly decreased, but the mean corpuscular hemoglobin ($p < 0.01$) and mean corpuscular hemoglobin concentration ($p < 0.001$) significantly increased in the males in the 1,800 ppm group. In the males in the 50 ppm group, white blood cell and platelets significantly decreased, whereas the mean corpuscular volume, mean corpuscular hemoglobin concentration and red cell volume distribution width significantly increased. Table 8 shows that the mean corpuscular volume significantly decreased ($p < 0.05$) in females in the 300 ppm group and decreased ($p < 0.001$) in females in the 1,800 ppm group. The red cell volume distribution width significantly decreased ($p < 0.001$) in females in the 50 ppm and 1,800 ppm groups.

Table 5. Relative organ weights of male SD rats after inhalation of 1-BP for 8 weeks

Unit: mg/100 g B.W.

Organ	Group 0 (Control)	Group 1 (50 ppm)	Group 2 (300 ppm)	Group 3 (1,800 ppm)
Thymus	114.1 ± 15.28	108.0 ± 20.87	95.8 ± 25.51	100.4 ± 24.22
Adrenal R	7.9 ± 1.62	9.1 ± 1.76	10.2 ± 2.71*	9.3 ± 2.54
Adrenal L	7.5 ± 1.45	9.8 ± 2.76*	10.3 ± 1.19**	9.3 ± 2.04*
Testis R	444.2 ± 22.17	422.5 ± 28.80	459.3 ± 54.80	471.3 ± 26.52*
Testis L	442.1 ± 27.18	423.1 ± 29.76	463.1 ± 50.27	476.1 ± 31.22**
Heart	338.9 ± 27.16	326.2 ± 16.89	348.1 ± 23.09	348.2 ± 15.38
Lung R	167.9 ± 23.35	151.0 ± 11.77	165.3 ± 11.66	179.3 ± 30.38
Lung L	322.0 ± 32.03	285.0 ± 34.18	323.0 ± 20.47	321.8 ± 46.31
Kidney R	330.8 ± 19.64	326.4 ± 28.07	334.9 ± 17.66	371.2 ± 17.12**
Kidney L	331.0 ± 32.03	346.5 ± 22.66	350.3 ± 26.65	359.7 ± 16.98
Spleen	181.4 ± 17.96	175.1 ± 18.60	189.3 ± 14.51	176.0 ± 16.60
Liver	2,567.4 ± 110.80	2,628.7 ± 203.60	2,746.8 ± 197.70*	3,011.1 ± 133.90***
Brain	453.6 ± 37.96	458.0 ± 48.68	505.1 ± 31.73*	520.9 ± 31.72**

All values are the mean ± SD. Significant differences as compared with the control: *p<0.05; **p<0.01; ***p<0.001.

Table 6. Relative organ weights of female SD rats after inhalation of 1-BP for 8 weeks

Unit: mg/100 g B.W.

Organ	Group 0 (Control)	Group 1 (50 ppm)	Group 2 (300 ppm)	Group 3 (1,800 ppm)
Thymus	130.5 ± 13.58	107.6 ± 15.56*	116.5 ± 17.59	107.6 ± 21.78*
Adrenal R	18.7 ± 2.31	16.9 ± 1.81	17.6 ± 2.84	17.4 ± 3.37
Adrenal L	17.5 ± 2.19	19.5 ± 1.82	18.3 ± 1.58	17.8 ± 3.08
Ovary R	29.2 ± 5.83	29.7 ± 5.79	30.3 ± 3.10	37.0 ± 6.68*
Ovary L	27.0 ± 4.88	29.9 ± 3.99	30.4 ± 4.39	35.0 ± 6.75**
Heart	360.9 ± 22.37	363.4 ± 28.48	360.8 ± 29.13	382.9 ± 41.34
Lung R	219.7 ± 19.32	207.6 ± 24.11	223.3 ± 22.70	230.5 ± 22.82
Lung L	436.2 ± 51.03	414.7 ± 14.23	407.8 ± 20.67	439.8 ± 34.33
Kidney R	337.2 ± 21.80	316.7 ± 18.68	336.1 ± 23.46	371.6 ± 23.11*
Kidney L	314.2 ± 48.62	310.5 ± 25.16	323.9 ± 26.57	358.3 ± 19.71**
Spleen	214.4 ± 23.00	208.4 ± 22.22	219.6 ± 24.36	237.9 ± 31.27
Liver	2,391.8 ± 60.30	2,374.2 ± 70.60	2,454.0 ± 200.50	3,067.7 ± 121.30***
Brain	756.7 ± 34.75	711.0 ± 26.75	677.8 ± 38.39	722.0 ± 36.60

All values are the mean ± SD. Significant differences as compared with the control: *p<0.05; **p<0.01; ***p<0.001.

Blood biochemistry: Table 9 shows the biochemical serum values in male rats after inhalation of 1-BP for 8 weeks. Table 10 shows those in female rats. The levels of alanine transferase, aspartate aminotransferase and lactate dehydrogenase in the males were significantly decreased in the some treated groups. In the females there was also a significant decrease in the level of alanine transferase.

Histopathological findings: All treated rats showed

signs of cytoplasmic vacuolation in the hepatocytes around the central veins, but without dose-dependency. Tubular casts in kidney were observed in females in the 1,800 ppm group. No other tissues in any of the treated groups showed signs of toxicologic lesions.

Discussions

1-BP has a low ozone-depleting potential (0.006) and global warming potential (0.0001). In addition, it

Table 7. Hematological values in male SD rats after inhalation of 1-BP for 8 weeks

Items	Group 0 (Control)	Group 1 (50 ppm)	Group 2 (300 ppm)	Group 3 (1,800 ppm)
WBC	9.9 ± 2.29	7.5 ± 1.43*	8.2 ± 2.22	7.1 ± 1.42**
RBC	7.9 ± 0.33	7.2 ± 0.79	7.6 ± 0.53	7.3 ± 0.39**
HGB	15.9 ± 0.43	15.9 ± 0.86	15.7 ± 0.48	15.8 ± 0.38
HCT	46.6 ± 3.96	43.9 ± 3.59	43.7 ± 2.43	40.8 ± 2.11**
MCV	58.1 ± 2.54	61.5 ± 2.96**	57.4 ± 1.07	56.1 ± 0.92*
MCH	20.2 ± 0.90	22.3 ± 1.54**	20.7 ± 0.92	21.8 ± 1.01**
MCHC	34.9 ± 1.65	36.2 ± 1.33*	36.0 ± 1.08	38.9 ± 1.78***
PLT	953.5 ± 84.1	873.5 ± 71.0*	894.2 ± 153.4	926.3 ± 84.4
RDW	12.9 ± 0.68	14.9 ± 0.99***	13.2 ± 0.84	12.1 ± 0.49
PDW	8.1 ± 0.63	8.4 ± 0.39	7.8 ± 0.49	7.8 ± 0.26
MPV	7.8 ± 0.40	8.1 ± 0.33	7.8 ± 0.36	7.8 ± 0.20
% LYM	89.6 ± 5.91	89.7 ± 2.83	91.4 ± 3.43	87.7 ± 4.72
% NEU	10.0 ± 6.02	9.7 ± 2.54	8.1 ± 3.41	11.4 ± 4.77
% EOS	0.3 ± 0.48	0.5 ± 0.85	0.4 ± 0.53	0.8 ± 0.63
% MONO	0	0	0	0.1 ± 0.32

All values are the mean ± SD. Significant differences as compared with the control: *p<0.05; **p<0.01; ***p<0.001.

WBC, white blood cell count (10³/mm³); RBC, red blood cell count (10⁶/mm³); HGB, hemoglobin (g/dl); HCT, hematocrit (%); MCV, mean corpuscular volume (μ³); MCH, mean corpuscular hemoglobin (pg); MCHC, mean corpuscular hemoglobin concentration (%); PLT, platelets (10³/mm³); RDW, red cell volume distribution width (%); PDW, platelet volume distribution width (%); MPV, mean platelet volume (μ³); %NEU, % of neutrophils; %LYM, % of lymphocytes; % EOS, % of eosinophils; % MONO, % of monocytes.

Table 8. Hematological values in female SD rats after inhalation of 1-BP for 8 weeks

Items	Group 0 (Control)	Group 1 (50 ppm)	Group 2 (300 ppm)	Group 3 (1,800 ppm)
WBC	4.7 ± 1.22	5.4 ± 0.91	5.1 ± 1.44	5.4 ± 1.12
RBC	7.3 ± 0.52	7.4 ± 0.58	7.2 ± 0.34	7.4 ± 0.49
HGB	15.5 ± 0.63	15.5 ± 0.97	15.3 ± 0.89	15.3 ± 0.79
HCT	44.1 ± 2.74	44.0 ± 3.06	42.8 ± 1.89	42.5 ± 2.46
MCV	60.4 ± 1.24	59.6 ± 1.03	59.4 ± 1.25*	57.3 ± 1.21***
MCH	21.3 ± 0.89	21.0 ± 0.98	21.3 ± 1.28	20.7 ± 1.82
MCHC	35.2 ± 1.04	35.2 ± 1.21	35.8 ± 1.66	36.2 ± 3.03
PLT	972.9 ± 58.1	913.6 ± 64.9	964.1 ± 80.8	928.9 ± 78.9
RDW	13.3 ± 0.50	11.8 ± 0.51***	13.4 ± 0.76	11.4 ± 0.48***
PDW	7.9 ± 0.24	7.8 ± 0.30	7.9 ± 0.33	7.8 ± 0.42
MPV	7.8 ± 0.15	7.8 ± 0.25	7.8 ± 0.31	7.8 ± 0.22
% LYM	92.2 ± 3.58	94.6 ± 2.41	90.3 ± 3.34	89.0 ± 5.31
% NEU	7.0 ± 3.33	4.5 ± 2.17	8.8 ± 3.05	9.5 ± 5.28
% EOS	0.8 ± 1.14	0.6 ± 0.84	0.9 ± 0.99	1.5 ± 1.08
% MONO	0	0	0	0

All values are the mean ± SD. Significant differences as compared with the control: *p<0.05; **p<0.01; ***p<0.001.

WBC, white blood cell count (10³/mm³); RBC, red blood cell count (10⁶/mm³); HGB, hemoglobin (g/dl); HCT, hematocrit (%); MCV, mean corpuscular volume (μ³); MCH, mean corpuscular hemoglobin (pg); MCHC, mean corpuscular hemoglobin concentration (%); PLT, platelets (10³/mm³); RDW, red cell volume distribution width (%); PDW, platelet volume distribution width (%); MPV, mean platelet volume (μ³); %NEU, % of neutrophils; %LYM, % of lymphocytes; % EOS, % of eosinophils; % MONO, % of monocytes.

Table 9. Biochemical serum values in male SD rats after inhalation of 1-BP for 8 weeks

Items	Group 0 (Control)	Group 1 (50 ppm)	Group 2 (300 ppm)	Group 3 (1,800 ppm)
TP	6.7 ± 0.44	6.5 ± 0.42	6.5 ± 0.38	6.2 ± 0.68
BUN	16.0 ± 1.46	15.2 ± 1.72	14.5 ± 0.91*	15.8 ± 2.17
CRTN	0.6 ± 0.11	0.6 ± 0.03	0.6 ± 0.03	0.6 ± 0.10
T-BIL	0.2 ± 0.16	0.2 ± 0.12	0.2 ± 0.10	0.2 ± 0.11
GLU	163.1 ± 20.90	154.2 ± 28.70	164.5 ± 14.20	164.3 ± 11.80
T-CHO	88.3 ± 17.70	92.9 ± 12.30	95.6 ± 17.90	81.2 ± 18.20
AST	112.8 ± 10.70	103.0 ± 28.90	81.4 ± 17.90***	80.3 ± 9.63***
ALT	44.0 ± 5.73	34.7 ± 6.25*	29.7 ± 8.56***	23.2 ± 6.78***
LDH	1,441.4 ± 623.70	1,168.7 ± 406.10	992.4 ± 657.90	1,067.9 ± 269.50*
ALP	214.9 ± 31.60	200.8 ± 35.00	180.5 ± 39.10	171.1 ± 54.00

All values are the mean ± SD. Significant differences as compared with the control: *p<0.05; **p<0.01; ***p<0.001.

TP, total protein (mg/dl); BUN, urea nitrogen in blood (mg/dl); CRTN, creatinine (mg/dl); T-BIL, total bilirubin (mg/dl); GLU, glucose (mg/dl); T-CHO, total cholesterol (mmol/l); AST, aspartate aminotransferase (μl); ALT, alanine aminotransferase (μl); LDH, lactate dehydrogenase (μl); ALP, alkaline phosphatase (μl).

Table 10. Biochemical serum values in female SD rats after inhalation of 1-BP for 8 weeks

Items	Group 0 (Control)	Group 1 (50 ppm)	Group 2 (300 ppm)	Group 3 (1,800 ppm)
TP	6.4 ± 0.22	6.5 ± 0.14	6.0 ± 0.71	6.5 ± 0.74
BUN	15.1 ± 1.80	16.7 ± 2.21	16.0 ± 2.54	15.4 ± 2.45
CRTN	0.7 ± 0.02	0.7 ± 0.03	0.7 ± 0.03	0.6 ± 0.07**
T-BIL	0.3 ± 0.08	0.3 ± 0.16	0.3 ± 0.11	0.21 ± 0.08*
GLU	136.1 ± 23.70	132.4 ± 30.90	160.4 ± 18.30*	144.0 ± 17.10
T-CHO	102.2 ± 25.40	88.0 ± 14.20	81.4 ± 15.40*	84.9 ± 33.80
AST	86.7 ± 17.60	100.1 ± 12.90	78.7 ± 20.10	83.0 ± 24.40
ALT	39.8 ± 19.10	29.1 ± 8.67	25.4 ± 5.89*	22.6 ± 3.09*
LDH	1,023.1 ± 164.70	1,037.5 ± 361.10	759.9 ± 205.80**	1,126.9 ± 189.20
ALP	135.4 ± 21.30	140.6 ± 40.40	135.6 ± 33.80	125.5 ± 24.60

All values are the mean ± SD. Significant differences as compared with the control: *p<0.05; **p<0.01; ***p<0.001.

TP, total protein (mg/dl); BUN, urea nitrogen in blood (mg/dl); CRTN, creatinine (mg/dl); T-BIL, total bilirubin (mg/dl); GLU, glucose (mg/dl); T-CHO, total cholesterol (mmol/l); AST, aspartate aminotransferase (μl); ALT, alanine aminotransferase (μl); LDH, lactate dehydrogenase (μl); ALP, alkaline phosphatase (μl).

has also good cleaning power⁽⁴⁾. Recently it has been used as an alternative cleaning solvent to CFC, hydrochlorofluorocarbon (HCEC), 1,1,1-trichloroethane (TCE) and 2-BP, all of which were associated with environmental and toxicologic problems.

Five groups of rats inhaled 0, 11,000 ppm, 13,000 ppm, 15,000 ppm and 17,000 ppm of 1-BP in acute inhalation toxicity tests. The LC₅₀ of 1-BP was estimated to be 14,374 ppm (95% confidence limit: 13,624–15,596 ppm).

This is lower than the LC₅₀ of 2-BP (31,171 ppm)⁽¹⁵⁾. 1-BP was shown to cause eye irritation with lacrimation in all the treated groups. No other abnormal clinical signs were observed due to exposure to 1-BP in four-hour inhalation. Body weight was similar in the control and treated groups. Gross findings on necropsy revealed no evidence of specific toxicity related to the 1-BP. No specific toxicologic lesions were observed on histopathological examination.

In repeated inhalation toxicity tests, no deaths occurred during the experiment. Clinical signs and gross findings on necropsy revealed no evidence of specific toxicity related to the 1-BP. Even though some items in treated groups were significantly different from those in the control group in urine biochemistry, hematology and blood biochemistry, they were mostly in the normal range. The relative organ weights of liver, the level of ALT, AST and LDH, and the observation of the cytoplasmic vacuolation in the hepatocytes around the central veins in both sexes of rats in the 1,800 ppm group appear to be related with the hepatotoxic effect of 1-BP, but which has no exposure effect relationship^{16, 17)}.

2-BP was reported to have specific reproductive and hematopoietic toxicity in both male and female SD rats after intraperitoneal injection, and in male Wistar rats after inhalation²⁻⁶⁾. 2-BP could also impair the bone marrow, resulting in pancytopenia^{5, 6)}. In this experiment the relative weights of testis and ovary in the 1,800 ppm 1-BP group were significantly increased, but there was no abnormality of testis or ovary in necropsy findings. 1-BP did not reveal specific lesions in testis or ovary histopathologically.

In conclusion, 1-BP was confirmed to have a low LC_{50} (4 h) of 14,374 ppm. 1-BP may be used as an alternative cleaning solvent in industry after getting specific and long-term toxicologic information on carcinogenicity and teratogenicity.

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