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Research Article

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Hepatotoxic Effect of Propylene Glycol Based Fog on Wistar Rats

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Abstract Theatrical fog is produced by a fog-machine which vaporizes a propylene glycol and water mixture (fog liquid). On leaving the machine and mixing with the cool external air, the vapor condenses and forms a dense fog. This fog finds application in the professional entertainment industry, fire service, armed forces and in churches for different purposes. Therefore, this inhalation toxicology study investigated the potential health effects of theatrical fog on wistar rats. A total of ninety female wistar rats were used for the study; Thirty rats each for acute (14 days), sub chronic (3 months) and chronic (6 months) studies respectively. Each set of 30 wistar rats was divided into 6 groups. While groups 2 to 5were exposed by whole body in a chamber to theatrical fog at the concentrations (15, 30, 60, 120 & 240 g/m^3), 2 hours daily, 3 days per week for sub chronic and chronic studies respectively. Group 1 served as control. In the acute study the animals were exposed 2 hours daily for 14 days. The animals were sacrificed under chloroform anesthesia at the expiration of each of the study intervals and blood samples collected for biochemical analysis. The results obtained from the acute study showed significant change in ALT level. The data gathered from the sub chronic study also depicted dosage independent statistically significant elevations in the plasma levels of AST, ALT and TB respectively. The chronic study also revealed significant alterations in the plasma concentrations of; AST, ALT, TB and CB correspondingly. In conclusion, the finding from this study shows that propylene glycol based fog appears to be deleterious to the liver.

Keywords Special-effect, pyrotechnics, hygroscopic, humectants, vaporizers, propylene glycol, fog

Introduction

Theatrical-fog is a dense fog ejected by a fog-machine. Generally, the machine vaporizes a glycol and water based liquid (fog liquid). On leaving the fogger and mixing with the cool external air, condensation occurs, producing a dense fog [1], This synthetic fog is commonly employed in the professional entertainment industries for creation of special effects for enhancement of the visibility of lighting and lighting effect and for generation of a particular sense of mood. It is the application of theatrical fog that causes the audience in entertainment venues to detect rays of light cutting across the auditorium [1]. In the armed forces, theatrical fog is used for troop's movement concealment at training and at warfare. In fire service it is applied during exercise. Theatrical fog also finds application in e -cigarette with a similar technique of production [2]. Nowadays people are creating special effect in several ceremonies including Church service, Christmas, weddings, birthdays, funerals and similar events. However, it is actually true that theaters are beautified by special effect but the safety of propylene glycol theatrical fog and the thermal decomposition products of propylene glycol; (acrolein, acetaldehyde and

formaldehyde, [3] are yet to be ascertained beyond doubt. Smoke effect denotes stage effect generated by pyrotechnic materials like smoke-cooky and cartridges; or some other inflammable stuffs such as incense. Smoke is distinguished from other special effects as it consists of solid tiny pieces discharged in the combustion process [1]. However, fog effect is produced by pumping one of the various glycols and water mixtures (fog fluids) into a heating compartment of the machine, basically a metal-block with a heating element, and heating until vaporization occurs, generating a dense opaque fog consisting of tiny liquid particles. The machines distinctively constructed to play this role are known as fog-machines or foggers.

Materials and Methods

Materials

Experimental Animals

Sixty (60) three week old wistar rats weighing (34-36g) were obtained from the Department of Pharmacology Animal House, University of Port Harcourt. Another 30 adult wistar rats weighing between (180 to 200g) were also obtained from same source. The rats were allowed to acclimatize for one week before the commencement of the study. The site temperature range was (20 to 25C^{o}) with relative humidity of (40 to 70 %) and 12hr light – 12hr dark sequence. Water and feed were provided ad libitum.

Test substance

The food grade propylene glycol used for fog-fluid formation for artificial-fog production for this research was obtained from Epoxy Oilserv. Nigeria limited, located at 238 Aba Expressway, Rivers state.

Fog-machine

The fog machine, Fog God, or Fogger – 1500 was acquired from Emmapee International, A subsidiary of De Absolute Sound Co. Ltd, a Nigerian distributor in Rivers State.

The fog – machine has a fog flow rate specification of (4000 cubic foot /min), heater 1500w and power input AV 220-240. It was operated manually or with a remote control.

Exposing Chamber

The exposing chamber with the volume (37.5 m^3) was carefully constructed with thick plywood to guard against sudden temperature and humidity rise during the experiment.

Fog concentration determination

The fog concentrations employed in this research was calculated with the formula;

$$\textbf{Fog concentration} = \frac{\textbf{X mg / m}^{\textbf{3}}\textbf{ / sec.}\times\ \textbf{T}}{\boldsymbol{Vm^3}}$$

Where **X mg / m^3 / sec.** is the machine's flow rate, **T** is the flow time while **Vm^3** is the volume of the exposing chamber.

The fog machine employed for this study had an output specification of (4000 grain/cubic foot/minute) which is equivalent to (9153407.6422629 mg/m^3) [4]

Therefore, the machine's output in grams/sec = $\frac{9153408}{60x1000}$

= 152.5568 g/ sec. (approx. 150 g /sec).

Exposure Technique

This study adopted the Organization for Economic cooperation and development OECD [5] protocol for Inhalation Study with modifications.

Methods

After acclimatization, the 60 rats were randomly divided into two sections with 30 animals for sub chronic and chronic studies. The 30 adult wistar rats formed a section for acute study.

Acute study

In this section 30 adult rats in six groups (A1, A2, A3, A4, A5, & A6) were used. While groups (A2, A3, A4, A5 & A6) were exposed by whole body to theatrical fog at the concentrations (15, 30, 60,120 & 240 g/m^3) 2 hours daily for 14 days, group A1 which was not exposed to the fog served as control.

Sub-chronic study

This section of the study consisted of 30 rats which were divided into 6 groups (S1, S2, S3, S4, S5 & S6) with 5 rats each. The five groups of rats in this section (S2, S3, S4, S5 & S6) were exposed to theatrical fog at the concentration range of (15, 30, 60, 120 & 240g/m^3) 2 hours daily, 3 days per week for 3 months. Group S1 was not treated with the fog and played the role of positive control.

Chronic Study

In this segment, while 5 groups, (C2 to C6) with 5 rats each were exposed to (15, 30, 60, 120 & 240g/m^3) 2 hours daily, 3 times per week for 6 months, group (C1) was not treated and played the role of a control.

Methods of data collection

At the end of 14 days for acute, 3 months for sub-chronic and 6 months for chronic studies, both the animals treated and the controls were sacrificed under chloroform anesthesia and blood samples were obtained through cardiac puncture for biochemical analysis.

Methods of statistical analysis

Data obtained from these tests were analyzed by application of SPSS version 20. A statistical tool, ANOVA was employed for comparing the means of the data obtained from various groups. The P- values less than 0.05 were considered significant. Where mean differences were significant, *post-hoc* test was performed with Turkey Honesty Significant Different (HSD) to compare various treatment groups with each other and with the control group.

Approval

This research was endorsed by the University of Port Harcourt research ethics committee.

Results

Table 1: Hepatic parameters following acute exposure to pg fog at different doses

Parameters	Control	15g/m^3	30g/m^3	60g/m^3	120g/m^3	240g/m^3
AST	28.00±4.00	38.67±5.69	28.00±2.00	27.67±4.04	33.00±9.00	33.67±.7.02
ALT	4.67±0.15	13.63±1.21**	9.53±1.80**	8.30±3.87**	6.40±2.62**	8.10±3.21
ALP	58.33±12.50	80.67±10.12	65.67±14.22	73.33±10.69	62.67±7.77	77.67±7.11
ALB	42.67±2.52	45.33±1.53	42.00±2.65	41.33±1.53	42.33±4.51	45..33±2.52
TB	5.60±0.80	8.00±0.92	5.67±0.45	6.13±0.70	6.73±2.12	6.67±1.39
CB	3.40±0.63	5.60±0.63	4.13±0.40	3.67±0.42	4.50±1.70	4.87±1.11

The results are expressed as M ± SD. * expresses significance at P value < 0.05 compared with the control.

Table 2: Hepatic parameters following sub chronic exposure to pg fog at different doses

Parameters	Control	15g/m^3	30g/m^3	60g/m^3	120g/m^3	240g/m^3
AST	28.00±4.00	27.50±6.36**	61.67±0.18**	55.50±3.54**	32.60±9.19**	23.50±.0.71
ALT	44.67±0.15	44.00±1.41	61.67±6.66**	53.00±1.41**	55.50±3.54**	56.50±2.12**
ALP	58.33±12.50	53.50±2.12	79.00±6.25	63.00±12.73	33.50±7.78	47.50±7.78
ALB	42.67±2.52	43.50±2.12	41.67±4.73	45.00±1.41	45.00±4.24	42..50±3.54
TB	5.60±0.80	10.10±0.85**	11.93±3.02**	10.85±0.51**	7.10±1.56**	5.15±0.51
CB	3.40±0.63	6.00±0.28	7.53±2.65	7.25±0.64	4.10±0.85	3.45±0.51

The results are expressed as M ± SD. * expresses significance at p value < 0.05compared with control.

Table 3: Hepatic parameters for chronic exposure to pg fog

Parameters	Control	15g/m^3	30g/m^3	60g/m^3	120g/m^3	240g/m^3
AST	28.00±4.00	27.68±5.69	28.00±2.00	85.50±17.68**	44.50±19.09**	32.50±.3.54**
ALT	4.67±0.15	13.63±1.21	8.52±1.80	79.50±6.36**	65.50±3.54**	63.00±4.24**
ALP	58.33±12.50	76.67±10.11	64.66±14.21	88.50±4.95	78.00±2.83	60.00±2.24
ALB	42.67±2.52	44.32±1.52	42.00±2.65	60.00±2.83	42.50±3.54	32..50±3.54
TB	5.60±0.80	6.00±0.82	5.67±0.45	16.60±2.69**	9.40±3.68	6.85±0.49
CB	3.40±0.63	4.60±0.62	3.50±0.40	12.50±1.84**	6.60±4.10**	3.90±0.85

The results are expressed as M ± SD. * expresses significance at P value <0.05 compared with the control.

Discussion of findings

This study assessed the potential effect of propylene glycol based fog on the liver. The result obtained from acute assessment showed significant change in alanine aminotransferase (ALT) plasma level. The data gathered from the sub chronic evaluation also recorded dose independent statistically significant elevations in the plasma levels of; aspartate aminotransferase (AST), alanine aminotransferase (ALT) and total bilirubin (TB) respectively. More so, the chronic study result also showed significant alterations in the plasma concentrations of; aspartate aminotransferase (AST),alanine aminotransferase (ALT), total bilirubin (TB) and conjugated bilirubin (CB).Our findings on hepatic effect of propylene glycol related fog appears to be at variance with Robbertson *et al* [6], and Venitz *et al* [7] who reported insignificant changes in liver enzymes. According to *"*Propionaldehyde Material Safety Data Sheet" (n.d.) chronic exposure to a metabolic product of propylene glycol, propionaldehyde, a potentially dangerous substance can cause liver injury. Also research on animals have shown that inhalation exposure to *propionaldehyde* culminated in anesthesia and *liver* damage and intra-peritoneal exposure caused elevation in blood pressure [8]. Also, Gage [9] reported vacuolization of hepatocytes following 6 hr daily for 6 days whole body exposure of female alderley-park rats to (1300ppm) propionaldehyde vapor. Furthermore, the substance, acrolein, one of the thermal decomposition products of propylene glycol have also been shown to be deleterious to many organs in the body including liver [10]. Therefore, based on these reports, the decline in the liver physiology recorded in this study may be regarded as the combined hepatic consequence of propionaldehyde and acrolein activities. There is a suggestion that acrolein is highly reactive in nature and binds rapidly to cellular components, hence many of the its toxicological effects may be due to saturation of protective cellular mechanisms (most notably glutathione) and subsequent reaction with critical sulfhydryl groups in proteins and peptides [11]. Some studies have revealed that pretreatment with compounds containing free sulfhydryl groups, for instance, cysteine, can ameliorate the acute lethality of acrolein [12]. Similarly, Eisenbrand *et al* [13] suggested that intracellular glutathione (or other free sulfhydryl groups) may protect against the deleterious effects of acrolein. In one study, acrolein and its glutathione adduct, glutathionylpropionaldehyde, induced oxygen radical formation [14].

Conclusion

In conclusion, the findings from this inhalational toxicity study have thrown more light on the impact of propylene glycol based fog. Propylene glycol based fog is injurious to the liver evidenced by induction of statistically significant elevations in the levels of plasma liver enzymes. Hence, need of propylene glycol based fog should go jointly with need for electronic fog monitor.

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