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Camphor elicits up-regulation of hepatic and pulmonary pro-inflammatory cytokines and chemokines via activation of NF-kB in rats

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ABSTRACT

Consumption of camphor infusions is widely used as an aphrodisiac in preparation for sexual intercourse, to boost performance. There is dearth of information associating or relating its consumption to liver or lung inflammation. Therefore, we investigated the effect of various doses of camphor in an acute study, on hepatic and pulmonary levels of some pro-inflammatory cytokines and chemokines in male wistar rats. Following administration, 2000 and 4000 mg/kg body weight camphor significantly increase liver and lung levels of tumor necrosis factor alpha (TNF-α), interleukin 1 beta (IL-1β) and interleukin 6 (IL-6) in a dose dependent manner compared with control, while interleukin 10 (IL-10) levels were significantly increased only by 1000 and 4000 mg/kg body weight camphor in liver and lung respectively, compared with control. Also compared with control, camphor administration resulted in a significant increase in the expressions of hepatic and pulmonary nuclear factor kappa B (NFkB), cyclooxygenase 2 (COX-2), regulated upon activation normal T cell expressed and secreted (RANTES) or CCL5, and monocyte chemo-attractant protein 1 (MCP-1) in a dose dependent manner. It is therefore advised that the use and consumption of camphor should be with caution as it could trigger liver and lung inflammation via activation of NF-kB and up-regulation of pro-inflammatory mediators.

1. Introduction

Camphor ($C_{10}H_{16}O$), a substance with strong aromatic odor is a waxy, transparent, white crystalline solid. It is gotten from *Cinnamomum camphora*, an evergreen tree found in Asia [1–3], and had also been synthetically produced from wood turpentine. It is a component of different types of foods, and common sources include herbs such as basil, sage, coriander, rosemary, and marjoram [4]. Camphor is utilized for diverse purposes including stimulation of respiratory and circulatory systems, cosmetics for external use, and psychological stimulation [5]. Also, it is utilized as a contraceptive, induction of abortion, for lowering milk formation in lactating women, and to enhance sexual activity [6,7]. Exposure to camphor can be via dermal route, inhalation, or ingestion [8].

Following exposure to camphor, metabolism is by cytochrome P_{450} [9], a class of heme-containing monooxygenases ubiquitously distributed in human and animal cells [10]. Hydroxylated metabolites of camphor formed following cytochrome P_{450} action are conjugated with glucuronic acid and passed out in urine [11]. Reports of toxicity have been documented in rats orally administered acute doses of camphor. Reduction in food consumption in a dose-dependent manner, weight reduction, piloerection and convulsion were reported symptoms of toxicity [12]. In primary culture of chick embryo hepatic cells, camphor resulted into an enhanced porphyrin accumulation ranging from 5 to 20-fold [13]. In a study conducted by Somade et al. [14], serum activity of lactate dehydrogenase was significantly increased, as well as tissue (liver, kidney, lung and testes) levels of endogenous antioxidant parameters (catalase, superoxide dismutase, and reduced glutathione) and malondialdehyde (a marker of lipid peroxidation) were significantly altered following administration of camphor in rats. Also in the same study conducted by Somade et al. [14], histopathology of the liver showed a severe portal congestion, and a very mild portal and central venous congestion. In lung, severe proliferation of alveolar pneumocytes, moderate proliferation of alveolar pneumocytes, generalized thickening of the alveolar walls due to

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moderate to severe proliferation of alveolar pneumocytes, diffuse thickening of the alveolar wall, thickened areas of the alveolar wall, with pink staining material in the lumina, and mild thickening of alveolar wall were revealed [14]. There is no substantive information associating or relating camphor administration to liver or lung inflammation. Therefore, we investigated the effect of camphor on hepatic and pulmonary levels of some pro-inflammatory chemokines (CCL5 and MCP-1) and cytokines (TNF-α, IL-1β, IL-6), as well as anti-inflammatory cytokine (IL-10) in male wistar rats.

2. Materials and methods

2.1. Test materials, kits and chemicals

Camphor (96% purity) is a product of Asia Camphor Manufacturing Co., China. Rat NF-kB, CCL5, COX-2, and MCP-1 monoclonal primary antibodies were purchased from Abcam UK; rat monoclonal secondary antibodies were purchased from Dako (Agilent Technologies, USA). All other used chemicals and reagents were of analytical grade, and were products of Sigma Chemical Co., Saint Louis, MO, USA or BDH Chemical Ltd, Poole, England. Rats TNF-α, IL-1β, IL-6, and IL-10 enzyme linked immunosorbent assay (ELISA) kits are products of Cusabio Technology llc, Houston, TX, USA.

2.2. Experimental animals and study design

Twenty (20) male wistar albino rats of an average weight of 200 g were used for this study. They were obtained from the animal house of the College of Veterinary Medicine, Federal University of Agriculture, Abeokuta, Nigeria. They were sheltered in steel metal cages in the animal house of our Department and were served food and water *ad libitum*. Experimental protocols were conducted in accord with guidelines of the Institutional Animal Care and Use Committee and were approved by the Animal Ethical Committee of the Department of Biochemistry, Federal University of Agriculture, Abeokuta, Nigeria. After 2 weeks of acclimatization, the rats were divided randomly into four groups of five animals each. Group I animals served as control and were orally administered 6 mL/kg olive oil, the vehicle for EC, while groups II, III and IV animals were orally administered 1000, 2000 and 4000 mg/kg camphor respectively based on calculated mean lethal dose (LD_{50}) in previous study [14].

2.3. Sample collections and preparations

Camphor was administered in specified doses at 24 h-interval for seven days, after which the animals were sacrificed by decapitation. They were treated in accordance with the international guide for the care and use of laboratory animals [15]. Liver and lung were harvested, washed in ice-cold saline (0.9% w/v) solution, blotted dry, and weighed. A section of the liver and lung was cut and fixed in 10% phosphate buffered formalin for immunohistochemistry. Another section of the liver and lung was suspended in ice-cold 0.1 M phosphate buffer (pH 7.4) for homogenization. Homogenization was followed by centrifugation at 5000 rpm for 10 min. The resulting supernatant was aliquoted into Eppendorf tubes and used for the estimations of TNF-α, IL-1β, IL-6, and IL-10.

2.4. Estimations of liver and lung levels of TNF-α, IL-1β, IL-6 and IL-10

Protocols in Cusabio ELISA kits (Cusabio Technology llc, Houston, TX, USA) were followed. Briefly, samples and standards were added into the wells already pre-coated with antibody specific for TNF-α, IL-1β, IL-6, or IL-10. Unbound substances were removed, and a biotin-conjugated antibody specific for TNF-α, IL-1β, IL-6, or IL-10 was added to the well. After washing, avidin conjugated Horseradish Peroxidase (HRP) was added to the wells, followed by addition of a substrate solution to give a color proportional to the amount of TNF-α, IL-1β, IL-6, or IL-10 bound in the initial step. Color development was stopped and intensity of the color was measured at 450 nm.

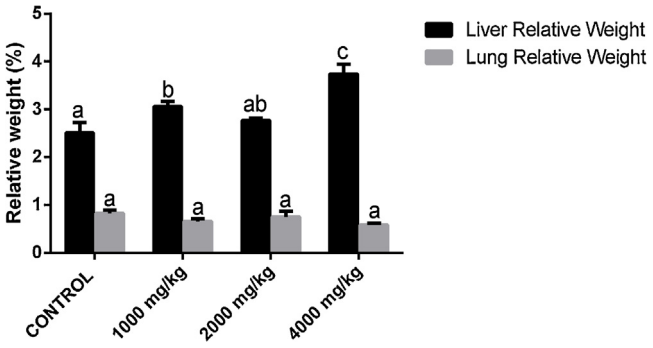

Fig. 1. Effect of camphor administration on liver and lung relative weights in rats. Values are expressed as mean ± standard error of mean (n = 5). Bars labeled with different superscript are statistically significant ($p < 0.05$).

2.5. Liver and lung immunohistochemistry

This was conducted as described by Ajayi et al. [16]. Poly-L-lysine charged slides were rehydrated in xylene as well as decreasing concentration of ethanol (100-50%). Heat-induced epitope retrieval was done in citrate buffer (pH 6.0) for 20 min followed by immersion in cold water for 10 min. Sections were marked with paraffin pen (PAP) and the endogenous peroxidase activities in the tissues were blocked with 5% hydrogen peroxide for 5 min in a dark cupboard. The sections were then incubated overnight at 4 °C with anti-NF-kB, anti−CCL5, anti−COX2 or anti-MCP-1 primary monoclonal antibodies. The slides were washed with Tris buffer saline and then incubated with Horseradish peroxidase labeled anti-rabbit monoclonal secondary antibodies (Dako, Agilent Technologies, US). Immune complexes were visualized using 0.05% 3, 3-diaminobenzidene (DAB), countered stained with hematoxylin and the slides were visualized under light microscope. Percentage of tissue-stained positive cells was scored.

2.6. Statistical analysis

Data were analyzed by one-way analysis of variance (ANOVA), followed by least significant difference (LSD) to test for significant differences among the groups of rats using Statistical Package for Social Sciences program version 17.0. Data were expressed as mean ± standard error of mean. P values less than 0.05 were considered statistically significant.

3. Results

3.1. Effect of camphor on liver and lung relative weights

As depicted in Fig. 1, administration of camphor (1000 and 4000 mg/kg) resulted in a significant increase ($p < 0.05$) in liver relative weight compared with control. In lung, no significant ($p > 0.05$) difference was recorded following camphor administration compared with control (Fig. 1)

3.2. Effect of camphor on hepatic TNF-α, IL-1β, IL-6, and IL-10

Liver levels of TNF-α (Fig. 2) and IL-6 (Fig. 4) were significantly ($p < 0.05$) increased in a dose dependent manner by 2000 and 4000

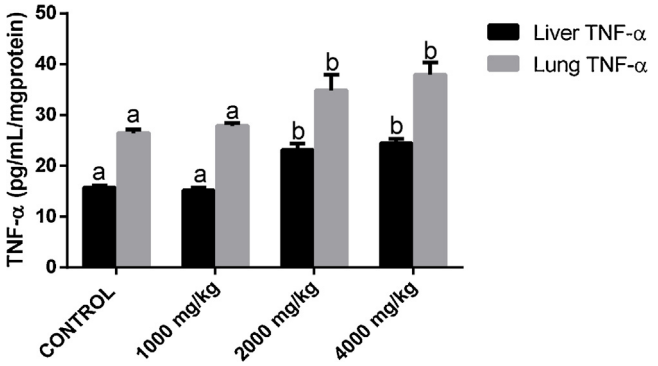

Fig. 2. Effect of camphor administration on hepatic and pulmonary levels of TNFα in rats. Values are expressed as mean ± standard error of mean. Bars labeled with different superscript are statistically significant ($p < 0.05$).

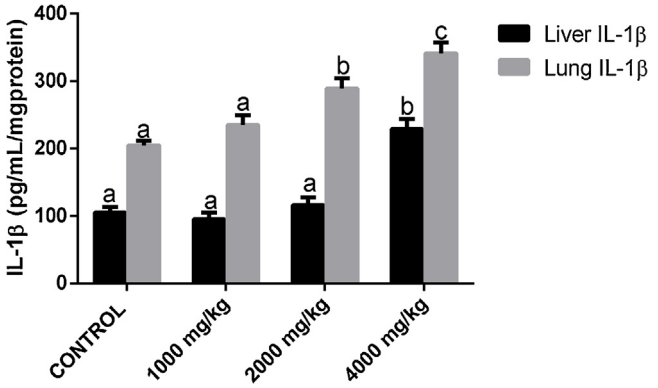

Fig. 3. Effect of camphor administration on hepatic and pulmonary levels of IL1β in rats. Values are expressed as mean ± standard error of mean. Bars labeled with different superscript are statistically significant ($p < 0.05$).

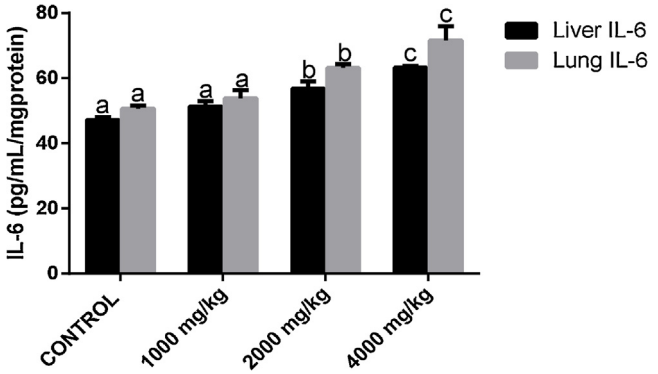

Fig. 4. Effect of camphor administration on hepatic and pulmonary levels of IL6 in rats. Values are expressed as mean ± standard error of mean. Bars labeled with different superscript are statistically significant ($p < 0.05$).

mg/kg body weight of camphor compared with control while liver IL-1β was only significantly ($p < 0.05$) increased in group administered 4000 mg/kg camphor (Fig. 3). IL-10 (Fig. 5) level was only significantly ($p < 0.05$) increased by 1000 mg/kg body weight of camphor compared with control.

3.3. Effect of camphor on pulmonary TNF-α, IL-1β, IL-6, and IL-10

Similarly in the lung, levels of TNF-α (Fig. 2), IL-1β (Fig. 3) and IL-6 (Fig. 4) were also significantly ($p < 0.05$) increased in a dose dependent manner by 2000 and 4000 mg/kg body weight camphor compared with control. Furthermore, there was a significant ($p <$

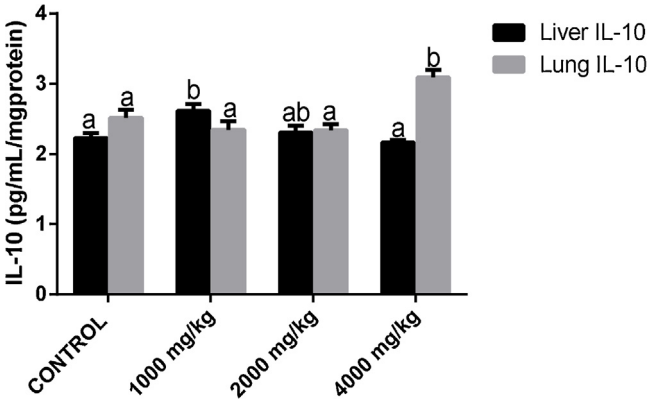

Fig. 5. Effect of camphor administration on hepatic and pulmonary levels of IL10 in rats. Values are expressed as mean ± standard error of mean. Bars labeled with different superscript are statistically significant ($p < 0.05$).

0.05) increase in the levels of IL-1β (Fig. 3) and IL-6 (Fig. 4) when group administered 4000 mg/kg body weight of camphor is compared with other tested doses (1000 and 2000 mg/kg body weight). For IL-10 (Fig. 5), the level was only significantly ($p < 0.05$) increased by 4000 mg/kg body weight camphor compared with control.

3.4. Effect of camphor on expressions of hepatic NF-kB, COX-2, CCL5 and MCP-1

There was a significant ($p < 0.05$) increase in the hepatic expressions of NFkB (Fig. 6A), COX-2 (Fig. 6B), RANTES (Fig. 6C), and MCP-1 (Fig. 6D) by all tested doses compared with control. Group administered 4000 mg/kg camphor showed the highest expressions of these parameters. The degree of expressions was 4000 mg/kg > 2000 mg/kg > 1000 mg/kg of camphor.

3.5. Effect of camphor on expressions of pulmonary NF-kB, COX-2, CCL5 and MCP-1

Similar trend was also recorded in the lung. All the tested doses of camphor resulted in a significant ($p < 0.05$) increase in the expressions of NFkB (Fig. 7A), COX-2 (Fig. 7B), RANTES (Fig. 7C), and MCP-1 (Fig. 7D) compared with control. Group administered 4000 mg/kg camphor also showed the highest expressions of the parameters, while the degree of expressions was also 4000 mg/kg > 2000 mg/kg > 1000 mg/kg of camphor.

4. Discussion

The present study investigated the effect of various doses of camphor in an acute study, on hepatic and pulmonary levels of some pro-inflammatory cytokines and chemokines in rats. The inflammatory response that occurs during chronic hepatic injury is a dynamic process with intra-hepatic accumulation of different immune cells (helper T cells, dendritic cells and macrophages) [17]. The recruitment and migration of these cells depend on the pattern of cytokines and chemokines that are produced by hepatocytes, endothelial cells, and biliary epithelial cells [18,19]. The significant increase in liver relative weight following camphor administration may be attributed to liver injury, leading to regeneration of damaged parts. Camphor is metabolized by the cytochrome P_{450} enzyme systems that are majorly localized in the liver, and this may explain the likelihood of camphor toxicity in the hepatocytes. The significant increase in liver relative weight recorded in this study corroborates our findings in previous study where a significantly increase the liver relative weight was also recorded in a dose dependent manner in camphor-induced hepatic oxidative stress

[14]. The non-significant increase in lung relative weight recorded in this study also corroborates the report in our previous study [14].

Cytokines are small secreted proteins produced by cells, and have a specific effect on the communications and interactions between cells [20]. Immune cells alternatively utilize transporters and ion channels to mediate the unconventional release of cytokines such as IL-1β [21–23] or influence their expression by reorienting ion balances within the cell nucleus [24,25]. Transient receptor potential (TRP) channels are broadly expressed and participate in the control of cell homeostasis. Hence, functional variations of TRP might be a key factor in the physiological recruitment of the immune response [26–28]. TRP vanilloid 3 (TRPV3) is seen in trigeminal ganglion (TG), nodose ganglion (NG), dorsal root ganglion (DRG) neurons, keratinocytes and certain parts of the brain that may be responsible for thermoregulation [29]. TRPV3 channel is activated by a wide range of monoterpenoids [30] including carvacrol [31], insensol [32], eugenol [31], camphor [33], and menthol [33], although these compounds can also

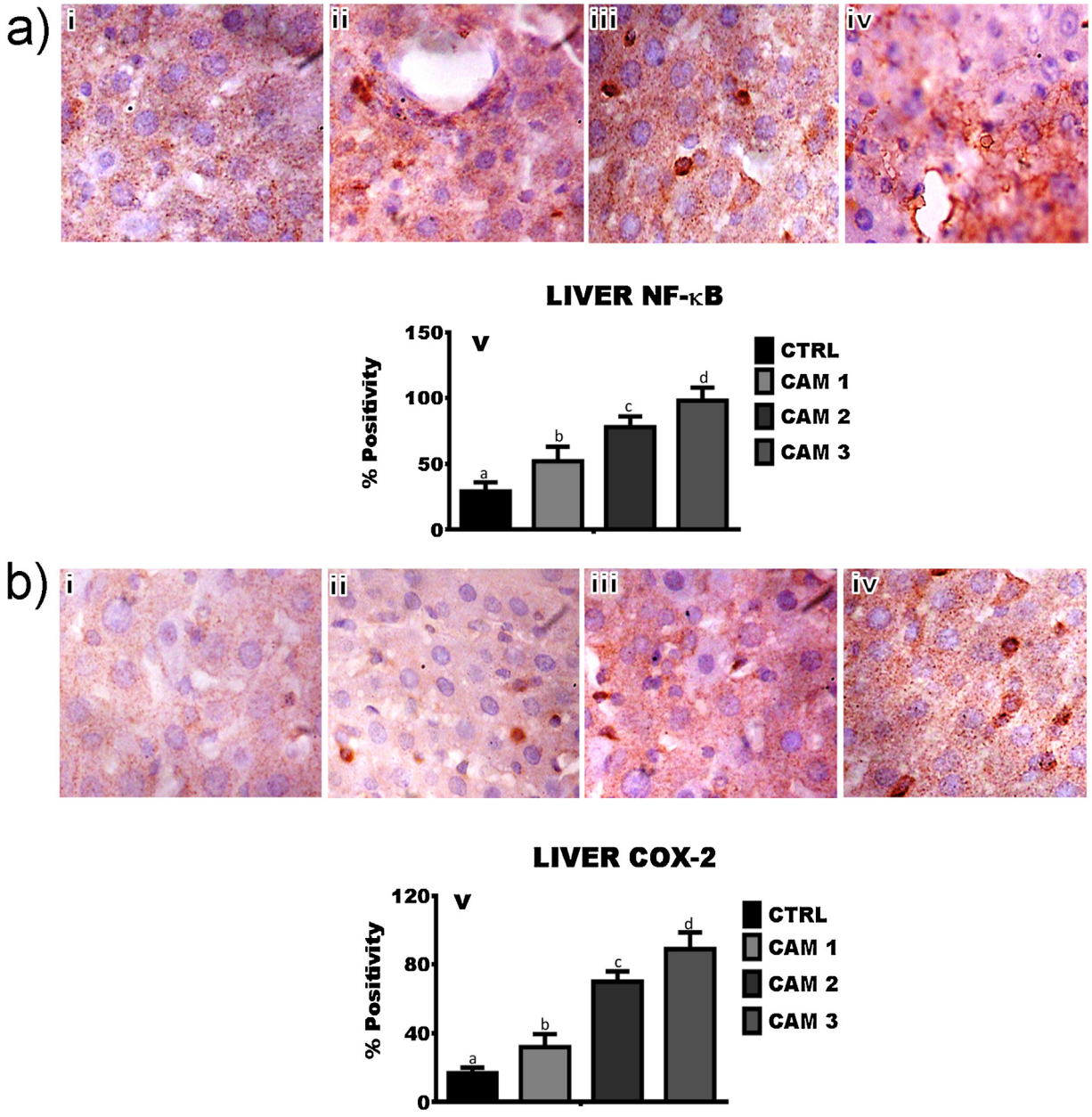

Fig. 6. A. Immuno–histochemical expressions of hepatic NFkB in camphor administered rats at 400 x magnification. i = control; ii = 1000 mg/kg camphor; iii = 2000 mg/kg camphor; iv = 4000 mg/kg camphor; v = graph showing percentage positive NFkB cells. Each bar represents mean ± SEM. Bars labeled with different superscript are statistically significant ($p < 0.05$). CTRL = control; CAM 1 = 1000 mg/kg camphor; CAM 2 = 2000 mg/kg camphor; CAM 3 = 4000 mg/kg camphor. **B.** Immuno-histochemical expressions of hepatic COX-2 in camphor administered rats at 400 x magnification. i = control; ii = 1000 mg/kg camphor; iii = 2000 mg/kg camphor; iv = 4000 mg/kg camphor; v = graph showing percentage positive COX-2 cells. Each bar represents mean ± SEM. Bars labeled with different superscript are statistically significant ($p < 0.05$). CTRL = control; CAM 1 = 1000 mg/kg camphor; CAM 2 = 2000 mg/kg camphor; CAM 3 = 4000 mg/kg camphor. **C.** Immuno-histochemical expressions of hepatic RANTES in camphor administered rats at 400 x magnification. i = control; ii = 1000 mg/kg camphor; iii = 2000 mg/kg camphor; iv = 4000 mg/kg camphor; v = graph showing percentage positive RANTES cells. Each bar represents mean ± SEM. Bars labeled with different superscript are statistically significant ($p < 0.05$). CTRL = control; CAM 1 = 1000 mg/kg camphor; CAM 2 = 2000 mg/kg camphor; CAM 3 = 4000 mg/kg camphor. **D.** Immuno-histochemical expressions of hepatic MCP-1 in camphor administered rats at 400 x magnification. i = control; ii = 1000 mg/kg camphor; iii = 2000 mg/kg camphor; iv = 4000 mg/kg camphor; v = graph showing percentage positive MCP-1 cells. Each bar represents mean ± SEM. Bars labeled with different superscript are statistically significant ($p < 0.05$). CTRL = control; CAM 1 = 1000 mg/kg camphor; CAM 2 = 2000 mg/kg camphor; CAM 3 = 4000 mg/kg camphor.

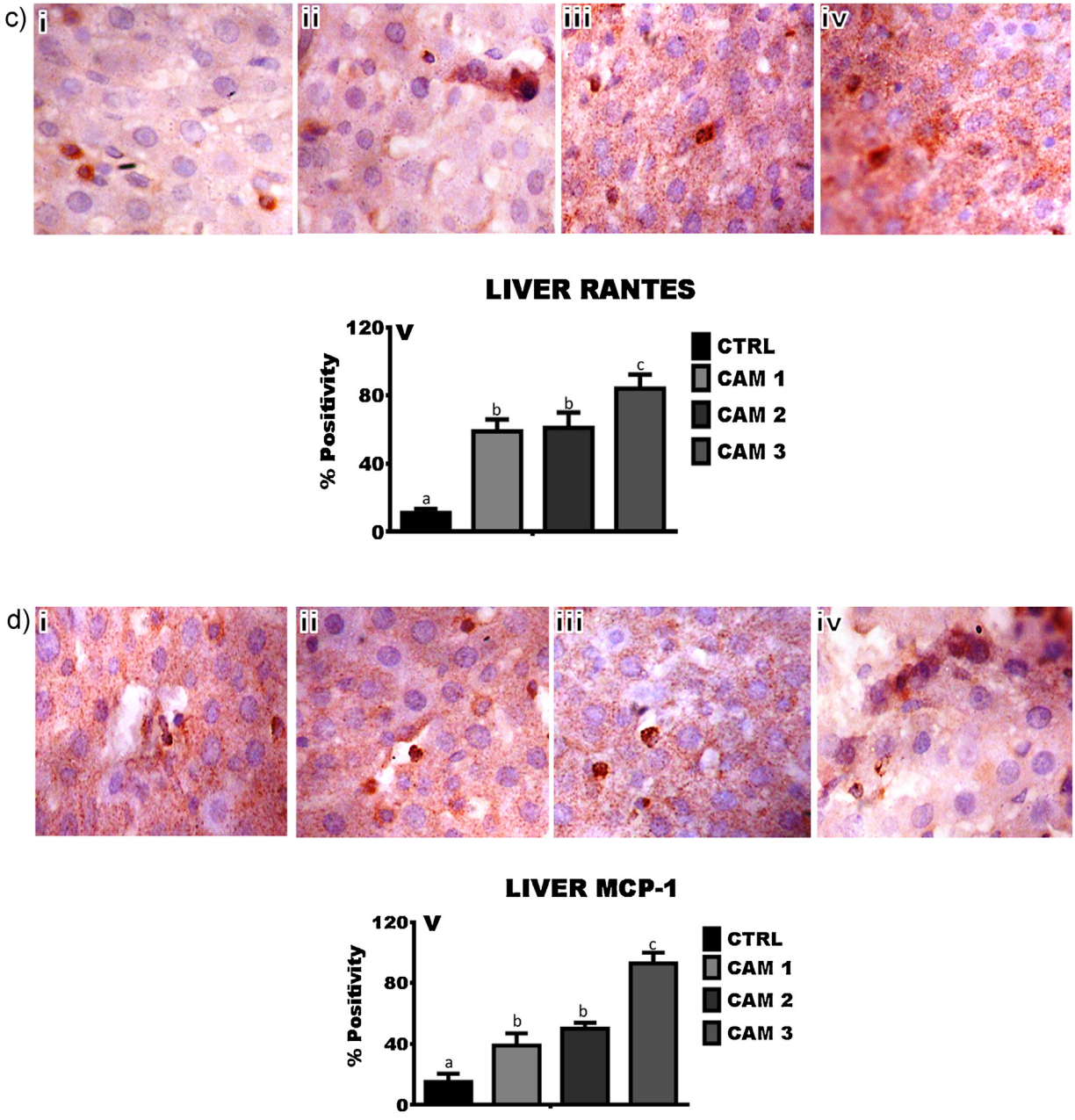

Fig. 6. (*Continued*)

be recognized by other TRP channels like TRP Ankyrin 1 and TRP Melastatin 8 [34]. In this study, the significant increase in the levels of hepatic and pulmonary TNF-α, IL-1β, IL-6 and IL-10 following administration of EC is an indication of liver and lung injury or infection causing their excretion and recruitment predominantly by the helper T cells and macrophages to the site of injury or infection where they promote inflammation and trigger pathological pain. Also, camphor being a monoterpenoid may have triggered the activation of the TRP ion channels in liver and lung, leading to the recruitment of immune response and subsequent release of the pro-inflammatory cytokines. It has been reported in some studies that ventilator-induced lung injury is characterized by the release of pro-inflammatory drivers (especially cytokines), alveolar and interstitial edema, infiltration of leukocytes, alveolar protein deposition, tissue disruption, and cellular necrosis [35,36]. Also in a study by Vaneker et al. [37], all measured cytokines and keratinocyte-derived chemokine levels increased progressively with mechanical ventilation duration in lung tissue. It is now widely accepted that high production of cytokines, especially TNF-α, IL-1β, IL-6, and IL-8 play an important role in initiating or executing lung injury [38–44]. Kupffer cells are the widest population of resident macrophages in liver and therefore play a pertinent role in immune-mediated liver toxicity and injury [45]. They have a major role in immune surveillance of the host and play a part in modulating systemic responses to chronic infections and controlling concomitant immune responses through antigen presentation and down-regulation of the activation and proliferation of T cells [46]. In their primary scavenging duty, kupffer cells engulf bacterial endotoxins and foreign particles, causing their activation and subsequent release of a number of modulators of cell signaling pathways, including reactive oxygen species, nitric oxide, eicosanoids, prostaglandins, peptide leukotrienes, and various cytokines like TNF-α, IL-1, and IL-6 [46]. In a recent study,

up-regulation of TNF-α following methyl methacrylate administration in rat was reported [47].

NF-kB belongs to a family of inducible nuclear transcription factors, which regulates a wide array of genes involved in various processes of inflammatory and immune responses [48]. The family is composed of five structurally related players, including NF-kB1 (p50), NF-kB2 (p52), RelA (p65), RelB and c-Rel, which coordinates transcription of target genes by binding to κB enhancer, a specific DNA element, as various hetero- or homo-dimers [49]. Activation of NF-kB involves two important signaling pathways. They are the canonical and noncanonical (or alternative) pathways, and are both important for regulating inflammatory and immune responses despite their disparities in signaling mechanism [50,51]. The canonical NF-kB pathway responds to various stimuli, such as ligands of various cytokine receptors, TNF receptor (TNFR) superfamily members, pattern recognition receptors (PRRs), as well as T-cell receptor (TCR) and B-cell receptor [52]. A well-known function of NF-kB is regulation of inflammatory responses, and in addition to coordinating the induction of various pro-inflammatory genes in innate immune cells, NF-kB also regulates the activation, differentiation

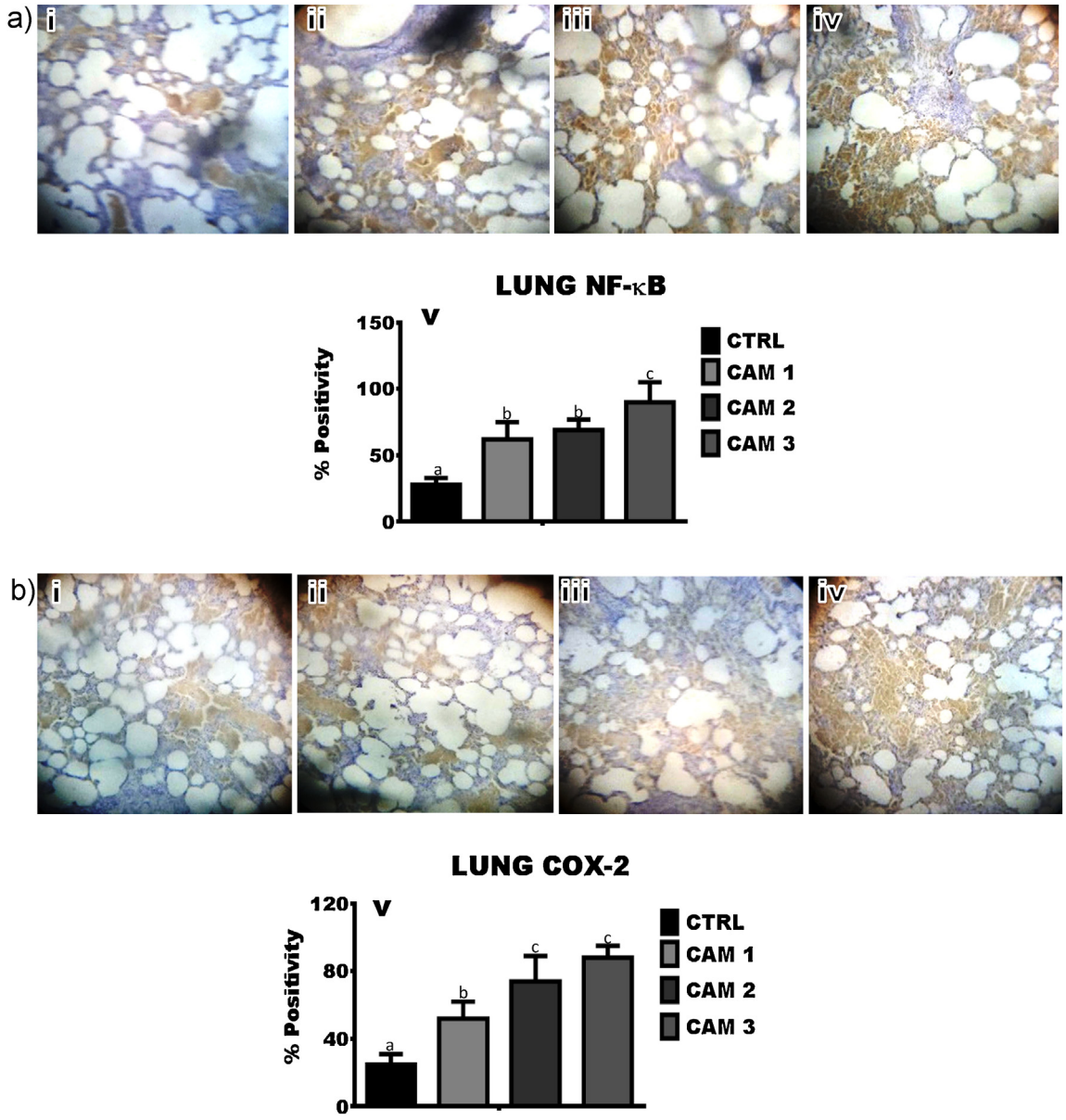

Fig. 7. A. Immuno–histochemical expressions of pulmonary NFkB in camphor administered rats at 40 x magnification. i = control; ii = 1000 mg/kg camphor; iii = 2000 mg/kg camphor; iv = 4000 mg/kg camphor; v = graph showing percentage positive NFkB cells. Each bar represents mean ± SEM. Bars labeled with different superscript are statistically significant ($p < 0.05$). CTRL = control; CAM 1 = 1000 mg/kg camphor; CAM 2 = 2000 mg/kg camphor; CAM 3 = 4000 mg/kg camphor. **B.** Immuno-histochemical expressions of pulmonary COX-2 in camphor administered rats at 40 x magnification. i = control; ii = 1000 mg/kg camphor; iii = 2000 mg/kg camphor; iv = 4000 mg/kg camphor; v = graph showing percentage positive COX-2 cells. Each bar represents mean ± SEM. Bars labeled with different superscript are statistically significant ($p < 0.05$). CTRL = control; CAM 1 = 1000 mg/kg camphor; CAM 2 = 2000 mg/kg camphor; CAM 3 = 4000 mg/kg camphor. **C.** Immuno-histochemical expressions of pulmonary RANTES in camphor administered rats at 40 x magnification. i = control; ii = 1000 mg/kg camphor; iii = 2000 mg/kg camphor; iv = 4000 mg/kg camphor; v = graph showing percentage positive RANTES cells. Each bar represents mean ± SEM. Bars labeled with different superscript are statistically significant ($p < 0.05$). CTRL = control; CAM 1 = 1000 mg/kg camphor; CAM 2 = 2000 mg/kg camphor; CAM 3 = 4000 mg/kg camphor. **D.** Immuno-histochemical expressions of pulmonary MCP-1 in camphor administered rats at 40 x magnification. i = control; ii = 1000 mg/kg camphor; iii = 2000 mg/kg camphor; iv = 4000 mg/kg camphor; v = graph showing percentage positive MCP-1 cells. Each bar represents mean ± SEM. Bars labeled with different superscript are statistically significant ($p < 0.05$). CTRL = control; CAM 1 = 1000 mg/kg camphor; CAM 2 = 2000 mg/kg camphor; CAM 3 = 4000 mg/kg camphor.

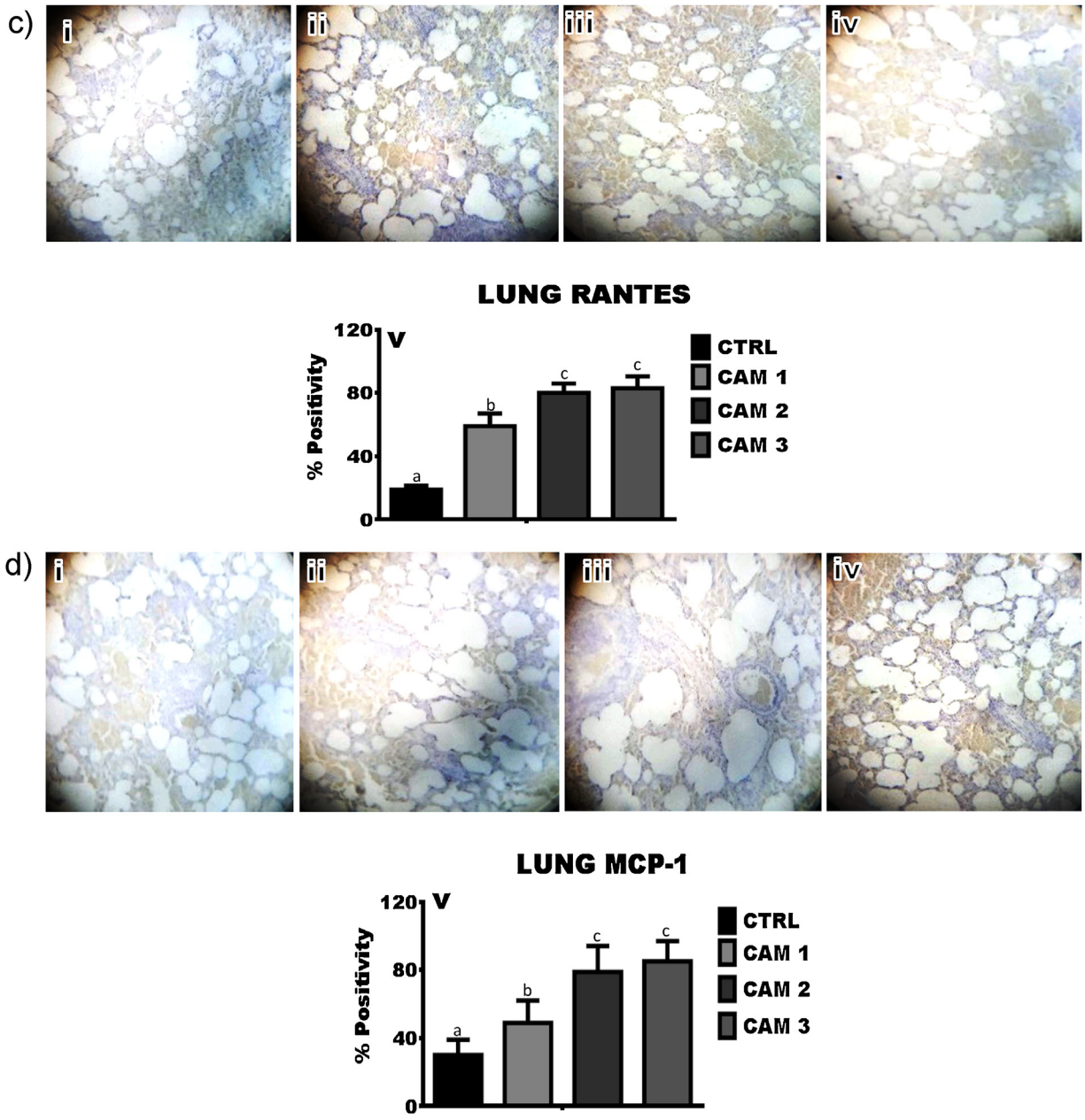

Fig. 7. (*Continued*)

and effector function of inflammatory T cells [53,54]. The significant increase in the expressions of hepatic and pulmonary NF-kB following administration may be attributed to camphor-induced toxicity, cytoplasmic NF-kB activation and its subsequent translocation to the nucleus to exert its pro-inflammatory genes transcription and expression roles.

Inflammatory response that occurs during chronic liver injury is a dynamic process with intrahepatic accumulation of diverse immune cells (macrophages, T cells and dendritic cells) [17]. Migration and positioning of these immune cells is determined by the pattern of cytokines and chemokines that are produced by hepatocytes, endothelial cells, and biliary epithelial cells [18,19]. Hepatic stellate cells have also been implicated in the recruitment of immune cells to the sites of tissue injury [55]. Activated stellate cells secrete great amounts of chemokines (CCL2, CCL3, CCL5, CCL11, CXCL8, CXCL9, and CXCL10), thus shaping the magnitude and the quality of the immune response during fibrotic liver diseases [55]. CCL5 (also known as RANTES), is a 7.8-kDa CC chemokine, which is highly expressed in the murine and human liver upon injury [56,57]. RANTES was initially considered a T cell–specific protein but has since been found to be produced by different cell types, including macrophages, endothelial, platelets, and stellate cells [58]. RANTES recruits NK cells, mast cells, T cells, dendritic cells, eosinophils, and basophils to sites of inflammation by interacting with 3 specific G protein–coupled receptors: CCR1, CCR3, and CCR5. CCR5 has been described on isolated liver stellate cells, indicating that these cells are a source and target of CCL5 within the liver [57,59]. MCP-1 (also called CCL2) on the other hand, is formed by diverse cell types, either constitutively or induction by cytokines, growth factors or oxidative stress [60]. It is produced by numerous cell types, including epithelial, smooth muscle, mesangial, astrocytic, monocytic, endothelial, fibroblasts, and microglial cells [61–64]. These cells are necessary for antiviral immune responses in the peripheral circulation as well as in tis-

sues. Macrophages/monocytes are the major source of CCL2 [65,66]. CCL2 regulates the migration and infiltration of memory T lymphocytes, natural killer (NK) cells, and monocytes [60]. Liver and lung expressions of CCL5 and MCP-1 in this present study following camphor administration may be as a result of damage to liver and lung tissues as well as NFkB activation which may have led to the expressions and recruitment of pro-inflammatory cytokines (TNF-α, IL-1β and IL-6) that in turn, coordinate the release of these pro-inflammatory chemokines (CCL5 and MCP-1) that selectively recruit neutrophils, lymphocytes, and monocytes to the site of tissue damage.

COX (also called prostaglandin H synthase) catalyses the first committed step in the biosynthesis of prostanoids, a broad family of arachidonate metabolites comprising prostaglandins, prostacyclins, and thromboxanes [67]. It is a peculiar enzyme, exhibiting 2 catalytic activities which are: a cyclooxygenase activity (which catalyses PGG_2 formation from arachidonic acid), and a peroxidase activity (which reduces PGG_2 to PGH_2). The peroxidase activity leads to the generation of free radicals, which are in part used by COX itself [67]. COX-2 is highly expressed in numerous cell types in response to cytokines, growth factors, and pro-inflammatory molecules and has become the isoform primarily responsible for prostanoid formation in acute and chronic inflammatory diseases [67]. Again, increased in the hepatic and pulmonary COX-2 expressions recorded in this study can be attributed to camphor-induced inflammation as evident by increased generation of pro-inflammatory cytokines reported in this study, which may have induced the increased expressions of COX-2 required to biosynthesize prostaglandins from arachidonate at the site of tissue damage or infection.

We therefore advise based on the outcomes of this study that the use and consumption of camphor should be with caution as it could trigger liver and lung inflammation via activation of NF-kB and up-regulation of pro-inflammatory mediators.

Declaration of Competing Interest

None.

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