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THE EFFECT OF GIVING DATE POWDER (PHOENIX DACTYLIFERA) ON HISTOPATHOLOGY OF PULMO ALVEOLI

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Abstract

Room deodorizer contains formaldehyde which can interfere with respiratory function through free radical activity. This impact can be reduced by antioxidants. Dates powder contains potent antioxidants. This study aims to reveal the effect of date palm powder on histopathology of the alveoli pulmo of Rattus norvegicus exposed to air freshener. The research subjects were 32 rats tested with a post-test only control group design which was divided into 8 groups. K0 was the control group, P was exposed to air freshener 4 hours/day, groups K1, K2, and K3 were given date palm powder (dose of 120 mg/kg, 240 mg/kg and 360 mg/kg), also PK1, PK2. , and PK3 which were exposed to room fresheners at the same time and treated with different doses of date palm powder. All groups were treated for 30 days then dissected and histopathologically observed alveoli pulmo. PK3 experienced significant improvement compared to P in terms of interalveolar septal thickness, alveolar dilatation, lymphocytes, neutrophils, and macrophages. P was significantly different from K0 in all parameters except eosinophils. Eosinophil cells in P, PK1, PK2, and PK3 increased compared to K0, although not significantly. Dates powder (Phoenix dactylifera) has a positive effect on the histology of the alveoli pulmo of Rattus norvegicus exposed to room fresheners by observing septal thickness, dilated alveolar diameter, and the number of inflammatory cells.

Keywords: Dates Powder, Air Freshener, Septal Thickness, Alveolar Diameter, Inflammatory Cells.

INTRODUCTION

Air pollution is a global problem that has not been resolved to date, even though increasing air pollution has a negative effect on breathing (Jeleńska et al., 2017). It is estimated that as many as 90% of urban people spend most of their time indoors (Spiru & Simona, 2017). Room deodorizer is one of the preferred sources of

air pollution because it smells good and fresh. Room deodorizer contains VOC (Volatile Organic Compounds) where one of the major components is formaldehyde.

Exposure to formaldehyde at certain concentrations causes irritation of the nose, eyes and throat (ATSDR, 1999). Exposure to formaldehyde disturbs the physiological balance of oxidant and antioxidant enzymes (Lino-dos-Santos-Franco et al., 2011). Dates have antioxidants and have a variety of medicinal properties (Tang et al., 2013). Dates contain important phytochemicals, including phenolics and flavonoids (R. M. A. Mohamed et al., 2014). In addition part of the fruit, date powder also contains antioxidants but only a few studies have discussed the composition of date powder. Dates powder contains vitamins A, C and E, amino acids, minerals and is not found starch or volatile substances. on the respiratory system.

RESEARCH METHODS

This experimental research was conducted using a post-test only control group design approach. The research subjects were 32 Rattus norvegicus aged 1 month. The test animals were kept in the biomedical test animal laboratory at the Faculty of Medicine and Health Sciences (FKIK) UMY. The grouping of subjects was done randomly with Simple Random Sampling. The eight groups were the control group (K0), negative control (P) induced by room deodorizer for 4 hours/day, three groups K1, K2, and K3 treated with date palm powder doses of 120, 240, and 360 mg/kg BW and three groups the PK1, PK2, and PK3 treatments which were induced by room deodorizers were simultaneously given date powder therapy with graded doses. The test animals were maintained for 30 days, then on the 31st day they were dissected. Histological preparations were made for the pulmo organs and then observed with a binocular microscope with a magnification of 40x10 in 10 fields of view. The results of the data were tested for normality using the Shapiro-Wilk method (sample <50). The data were normally distributed followed by analysis of the One Way Anova test and then Duncan's post hoc test. Meanwhile, the data were not normally distributed, so the analysis was carried out using the Kruskal-Wallis test and then continued with the Man-Whitney test.

RESULT AND DISCUSSION

The thickness of the interalveolar septum has p <0.05 indicating that the data is not normally distributed. Furthermore, data analysis was continued with the Kruskal-Wallis test. Obtained p <0.05 indicating there was a significant difference in the test group.

Table 1. Average score of interalveolar septum thickness (x ± SD) of Rattus norvegicus

Group	Average
Control (K0)	329.22 ± 2.72^{bc}
Fragrance (P)	251.18 ± 9.42^{a}
Date 1 (K1)	334.76 ± 13.94^{bc}
Dates 2 (K2)	371.30 ± 31.85^{c}
Dates 3 (K3	379.87 ± 10.31^{c}

Perfume and Dates 1 (PK1)	286.61±22.83[ab]
Perfume and Dates 2 (PK2)	332.22±10.34[bc]
Perfume and Dates 3 (PK3)	343.03±10.45[c]

Information a, b, c: different letters indicate a significant difference and the same letter indicates no significant difference in the Kruskal Wallis statistical test with a significance level of 95% Date 1 = 120 Kg/BB, Date 2 = 240 Kg/BB, Dates 3 = 360 Kg / BB

After the Mann-Whitney test, there was a significant difference between the K0 group and the P, PK1, and PK2 groups; then group P with groups K1, K2, K3, and PK3; K1 group with PK2 group; and the PK1 group with K1, K2, K3, PK2, and PK3. Below is a histological image of the white rat lung focused on the diameter of the alveoli and the interalveolar septum:

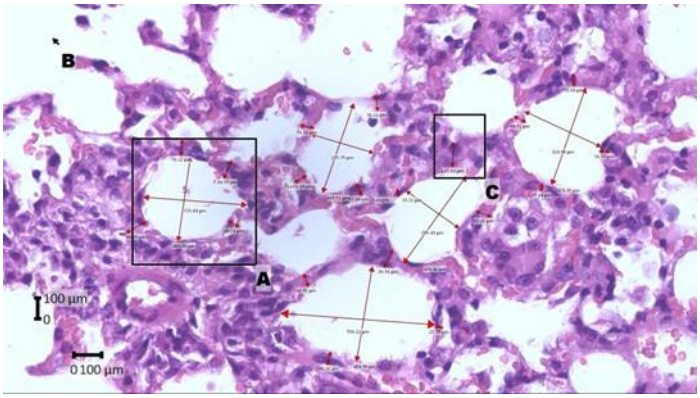

Figure 1. Histology of alveolar diameter and interalveolar septum in the control group (K0) which were not treated with air freshener or date powder, HE (10x40)
Description: A = Alveolus B = Saccus alveolus C = Septum interalveolaris

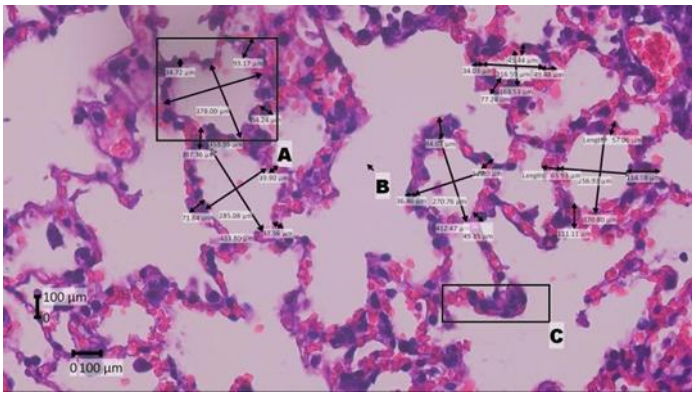

Figure 2. Histology of alveolar diameter and interalveolar septum in the air freshener group (P) treated with air freshener and date powder, HE (10x40)
Description: A = Alveolus B = Saccus alveolus C = Septum interalveolaris

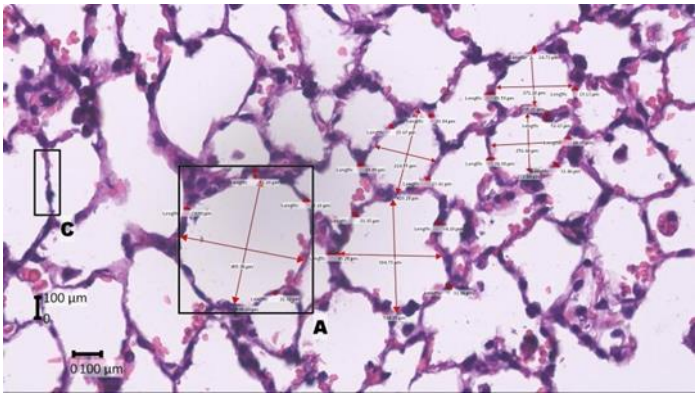

Figure 3. Histology of alveolar diameter and interalveolar septum interalveolaris in the treatment group of date palm powder dose of 120 mg/kgBB (K1), HE (10x40) Description: A = Alveolus B = Saccus alveolus C = Septum interalveolaris

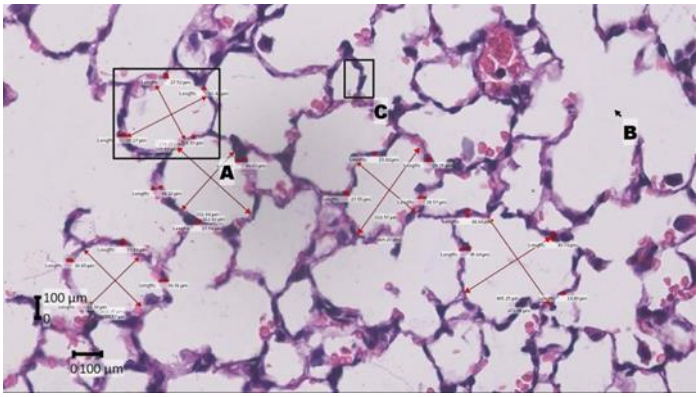

Figure 4. Histology of alveolar diameter and interalveolar septum interalveolaris in the treatment group of date palm powder dose of 240 mg/kgBB (K2), HE (10x40) Description: A = Alveolus B = Saccus alveolus C = Septum interalveolaris

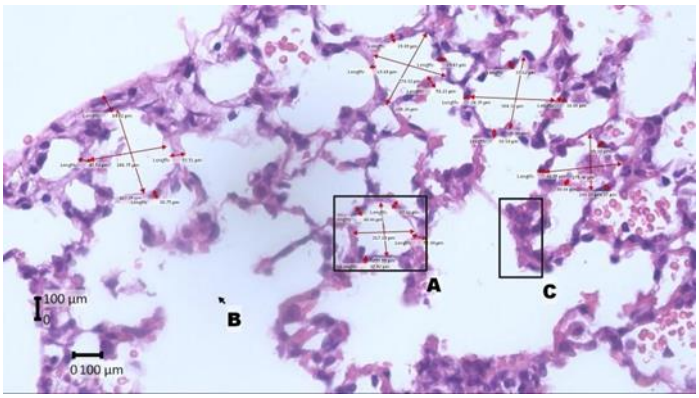

Figure 5. Histology of alveolar diameter and interalveolar septum interalveolaris treatment group of date palm powder dose of 360 mg/kgBB (K3), HE (10x40) Description: A = Alveolus B = Saccus alveolus C = Septum interalveolaris

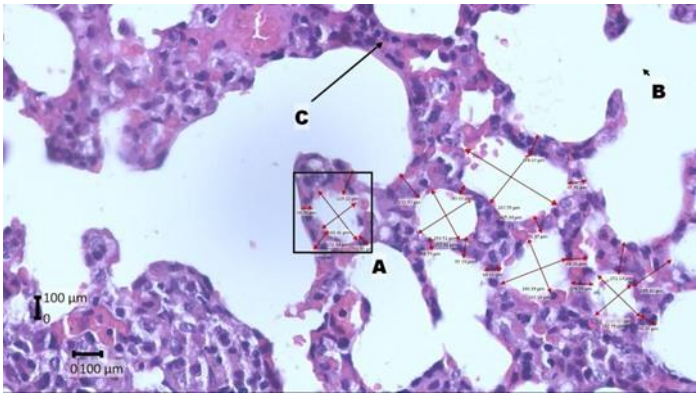

Figure 6. Histology of alveolar diameter and interalveolar septum interalveolaris treatment group of date palm powder dose of 120 mg/kgBB (K1), HE (10x40)
Description: A = Alveolus B = Saccus alveolus C = Septum interalveolaris

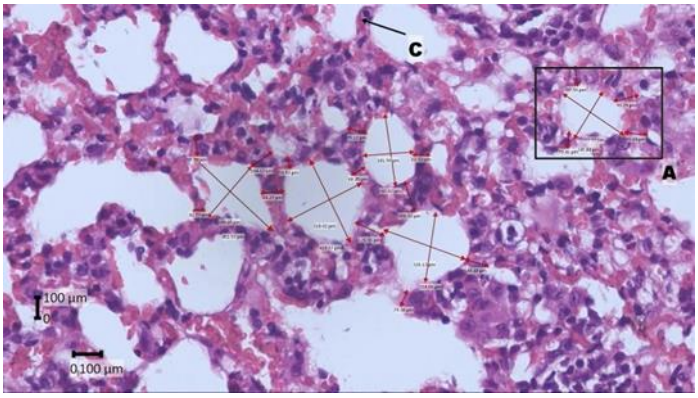

Figure 7. Histology of alveolar diameter and interalveolar septum interalveolaris treatment group of room deodorizer and date powder dose of 240 mg/kgBB (PK2), HE (10x40)
Description: A = Alveolus B = Saccus alveolus C = Septum interalveolaris

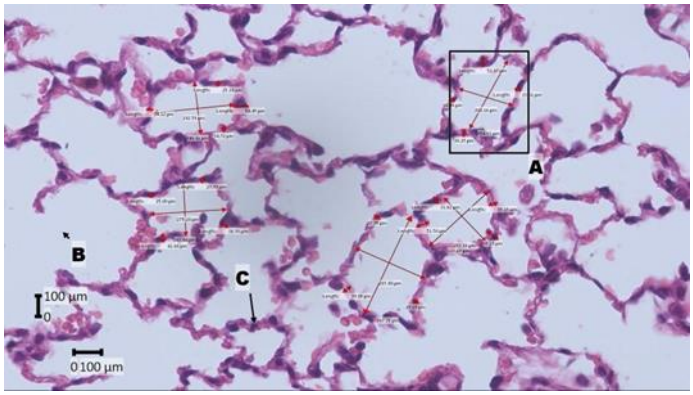

Figure 8. Histology of alveolar diameter and interalveolar septum interalveolaris treatment group of room deodorizer and date powder dose of 240 mg/kgBB (PK2), HE (10x40)
Description: A = Alveolus B = Saccus alveolus C = Septum interalveolaris

The diameter of the alveoli is measured by calculating the diameter of the inner side from the horizontal and vertical directions so that the average diameter is

obtained. After the normality test, the value of p> 0.05 was obtained, which means that the data distribution was normal. Data analysis was continued with the One-Way Anova method, and a value of p=0.000 or p<0.05 was obtained which indicated that there was a significant difference in alveolar diameter. The average alveolar diameter in micrometers (μm) can be seen in Table 2 below.

Table 2. Mean score of alveolar diameter (x ± SD) of Rattus norvegicus

Group	Average
Control (K0)	39.64±2.02[a]
Fragrance (P)	155.98±32.64[cd]
Date 1 (K1)	39.51±3.02[a]
Dates 2 (K2)	37.88±6.09[ab]
Dates 3 (K3	45.34±5.18[ab]
Perfume and Dates 1 (PK1)	113.52±10.87[d]
Perfume and Dates 2 (PK2)	64.55±9.63[bc]
Perfume and Dates 3 (PK3)	45.45±7.60[ab]

Information a, b, c: different letters indicate a significant difference and the same letter indicates no significant difference in the Kruskal Wallis statistical test with a significance level of 95% Date 1 = 120 Kg/BB, Date 2 = 240 Kg/BB, Dates 3 = 360 Kg/BB

Data analysis using Duncan's post hoc then found that the P group was significantly different from the K0, K1, K2, K3, PK2, and PK3 groups. Then there was no significant difference between the P and PK1 groups.

Furthermore, the data on inflammatory cells were tested for normality and showed that lymphocytes, neutrophils and macrophages each group had a p-value> 0.05, which means that the data were normally distributed. Then the three groups of inflammatory cells were tested parametric One Way Annova.

Table 3. Average lymphocytes and neutrophils (x ± SD) of Rattus norvegicus

Group	Average Number of Inflammatory Cells ± SD	
	Limfosit	Neutrofil
Control (C)	25.23±16.51[ab]	0.73±0.42[a]
Fragrance (P)	70.35±40.99[cd]	14.98±5.60[c]
Date 1 (K1)	18.13±8.6[ab]	1.50±1.28[a]
Dates 2 (K2)	11.15±3.89[a]	0.90±0.94[a]
Dates 3 (K3	32.93±22.06[abc]	2.20±1.91[ab]
Fragrance and	93.50±26.51[d]	5.55±2.55[b]
Dates 1 (PK1) Fragrance and	55.75±26.96[bcd]	4.33±1.69[ab]
Dates 2 (PK2) Fragrance and Dates 3 (PK3)	24.73±32.13[ab]	1.22±1.08[a]

Information a, b, c: different letters indicate significant differences and the same letters indicate no significant differences in the Kruskal Wallis statistical test with a significance level of 95%

Date 1 = 120 Kg/BB, Date 2 = 240 Kg/BB, Date 3 = 360 Kg/BB

Below shows inflammatory cells in pulmonary histology:

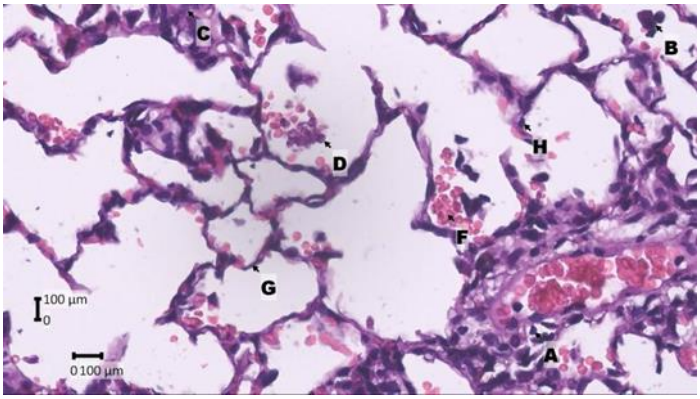

Figure 9. Pulmonary histology and the number of inflammatory cells in the control group (K0), HE (10x40)
Description: A = Lymphocytes; B = Macrophages; C = Neutrophils; D = Eosinophils; E = Emphysema; F = Red blood cells; G = Pneumocyst type 1; H = Pneumocyte type 2

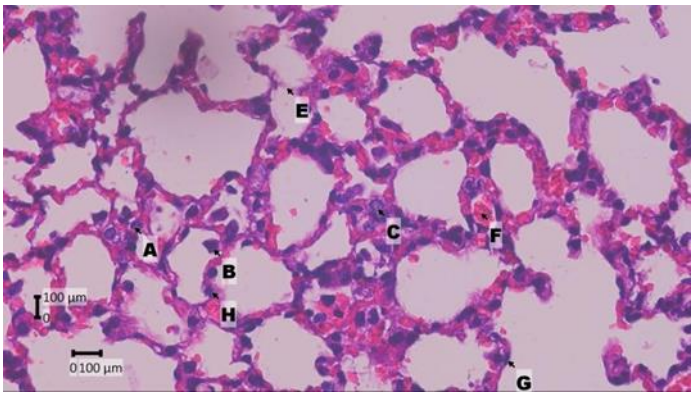

Figure 10. Histology of the lungs and the number of inflammatory cells in the air freshener treatment group (P), HE (10x40)
Description: A = Lymphocytes; B = Macrophages; C = Neutrophils; D = Eosinophils; E = Emphysema; F = Red blood cells; G = Pneumocyst type 1; H = Pneumocyte type 2

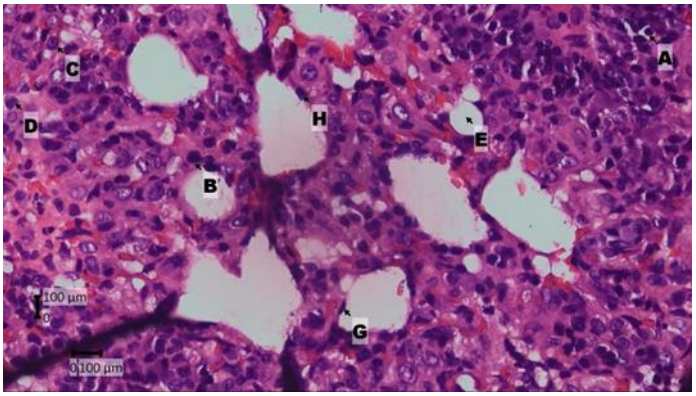

Figure 11. Histology of the lungs and the number of inflammatory cells in the date palm powder treatment group at a dose of 120 mg/kg BW (K1), HE (10x40)
Description: A = Lymphocytes; B = Macrophages; C = Neutrophils; D = Eosinophils; E = Emphysema; F = Red blood cells; G = Pneumocyst type 1; H = Pneumocyte type 2

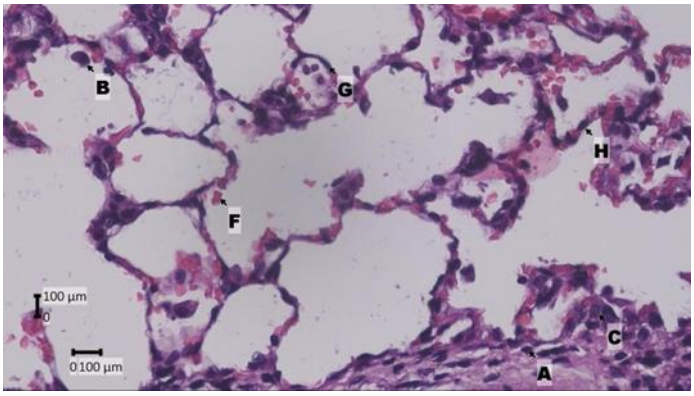

Figure 12. Histology of the lungs and the number of inflammatory cells in the date palm powder treatment group at a dose of 240 mg/kg BW (K2), HE (10x40)
Description: A = Lymphocytes; B = Macrophages; C = Neutrophils; D = Eosinophils; E = Emphysema; F = Red blood cells; G = Pneumocyst type 1; H = Pneumocyte type 2

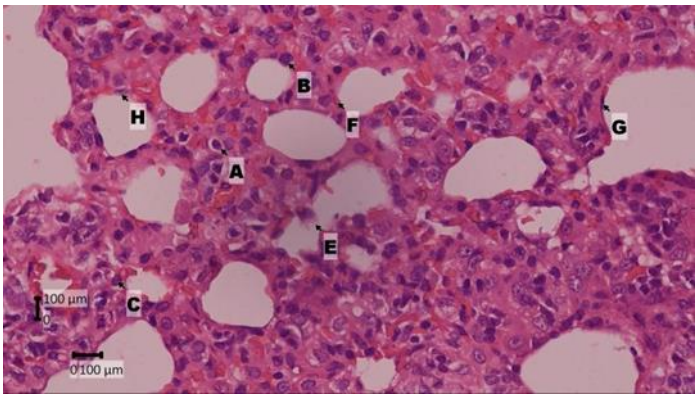

Figure 13. Histology of the lungs and the number of inflammatory cells in the date palm powder treatment group at a dose of 360 mg/kg BW (K3), HE (10x40)

Description: A = Lymphocytes; B = Macrophages; C = Neutrophils; D = Eosinophils; E = Emphysema; F = Red blood cells; G = Pneumocyst type 1; H = Pneumocyte type 2

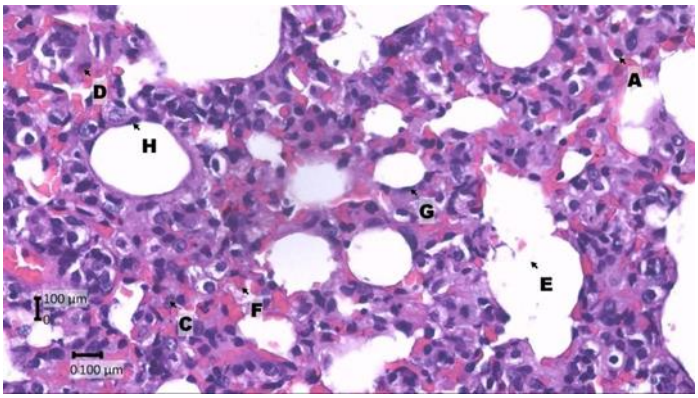

Figure 14. Histology of the lungs and the number of inflammatory cells in the air freshener group and the treatment with date palm powder dose of 120 mg/kgBB (PK1), HE (10x40) Description: A = Lymphocytes; B = Macrophages; C = Neutrophils; D = Eosinophils; E = Emphysema; F = Red blood cells; G = Pneumocyst type 1; H = Pneumocyte type 2

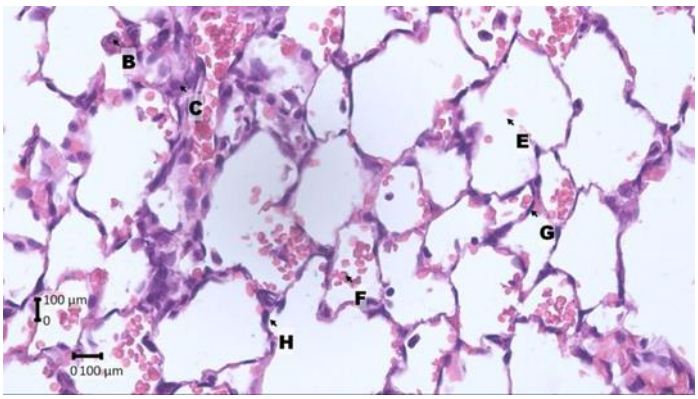

Figure 15. Histology of the lungs and the number of inflammatory cells in the room freshener and date powder treatment group at a dose of 240 mg/kg BW (PK2), HE (10x40) Description: A = Lymphocytes; B = Macrophages; C = Neutrophils; D = Eosinophils; E = Emphysema; F = Red blood cells; G = Pneumocyst type 1; H = Pneumocyte type 2

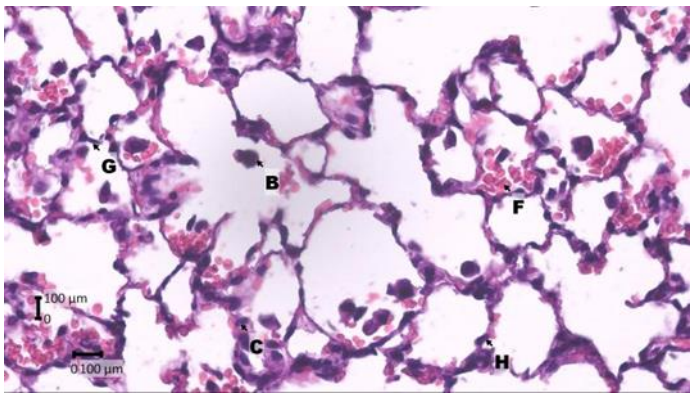

Figure 16. Histology of the lungs and the number of inflammatory cells in the room deodorizer and date powder treatment group at a dose of 360 mg/kgBB (PK3), HE (10x40) Description: A = Lymphocytes; B = Macrophages; C = Neutrophils; D = Eosinophils; E = Emphysema; F = Red blood cells; G = Pneumocyst type 1; H = Pneumocyte type 2

The results of the One Way Annova test obtained p = 0.000 in the lymphocyte cell group, p = 0.000 in the neutrophil cell group, and p = 0.001 in the macrophage cell group indicating that there was a significant difference (p <0.05) so that post-analysis could be continued. hoc Duncan.

In lymphocyte inflammatory cells, the K0 group was significantly different from the P and PK1 groups and not significantly different from the other groups. In the neutrophil inflammatory cell group, the K0 group also differed significantly from the P and PK1 groups. Then for macrophage inflammatory cells, the K0 group was significantly different from the PK3 group.

Whereas the eosinophil inflammatory cell group had normality which was not normally distributed, namely p <0.05, so the data was continued with the Kruskal Wallis parametric test. This analysis test yielded a value of p=0.167 or p>0.05 indicating that there was no difference in the average number of eosinophil cell groups.

Table 4. Mean eosinophil and macrophage cells (x ± SD) Rattus norvegicus

Group	Average Number of Inflammatory Cells ± SD	
	Eosinofil	**Makrofag**
Control (C)	0.08±0.15[a]	7.45±0.79abc
Fragrance (P)	0.60±0.80[a]	5.38±2.92[ab]
Date 1 (K1)	0.15±0.17[a]	10.00±1.86[cd]
Dates 2 (K2)	0.05±0.10[a]	8.30±1.56[cd]
Dates 3 (K3	1.10±1.17[a]	7.15±0.94abc
Perfume and Dates 1 (PK1)	1.18±1.56[a]	5.00±1.84[a]
Perfume and Dates 2 (PK2)	0.73±0.71[a]	8.17±1.78bcd
Perfume and Dates 3 (PK3)	0.13±0.15[a]	10.85±1.68[d]

Information a, b, c: different letters indicate significant differences and the same letters indicate no significant differences in the Kruskal Wallis statistical test with a significance level of 95%

Date 1 = 120 Kg/BB, Date 2 = 240 Kg/BB, Date 3 = 360 Kg/BB

Discussion

Changes in the size of the septum thickness cannot be separated from the mechanism of edema and the activity of reactive oxygen compounds. This change occurred significantly in group P (fragrances), PK1 (perfume and dates at a dose of 120 mg/kg BB), and PK2 (fragrances and dates at a dose of 240 mg/kgBB) with thicker septum compared to group K0 (control).

Even though the gel form of room deodorizer has a lower chemical content compared to other forms, there are still significant amounts of formaldehyde, naphthalene, xylene, cresol, and ethanol in it. vis by the UGM Integrated Research

and Testing Laboratory (LPPT). According to the Agency for Toxic Substances and Disease Registry, formaldehyde concentrations of 0.6 – 1.9 ppm in the air can cause nose and eye irritation, eczema, and changes in lung function.

Formaldehyde levels in the lungs were higher than in blood, brain, liver and kidney in rats exposed to formaldehyde. Formaldehyde is a potent respiratory tract irritant. Formaldehyde reacts directly on tissues and is cytotoxic. The mechanism of invasion of inflammation caused by inhalation of formaldehyde will increase the permeability of blood vessels in the airways of rats and cause microvascular leakage in the airways through stimulation of sensory nerves which then affect the tachykinin NK1 receptors. There is an increase in cellularity of the alveolar walls due to the proliferation of alveolar cells causing thickening of the alveolar septum in white rat histology (A. M. T. Mohamed, 2012). The loss of protein-rich fluid into the perivascular space increases the osmotic pressure of the interstitial fluid and decreases intravascular osmotic pressure. Water and ions will flow into the extravascular tissue and accumulate to become edema. This process will spur thickening of the interalveolar septum (Junqueira et al., 1995).

Another factor that causes thickening of the septum is exposure to formaldehyde which increases the activity of reactive oxygen compounds resulting in damage to the components of the cell membrane. Reactive oxygen species (ROS) are continuously formed in cells as a consequence of external factors and they become harmful when overproduced under abnormal conditions such as inflammation (Türkoğlu et al., 2008). It is known that increased free radical activity can cause tissue damage. In addition, there was a decrease in the activity of the enzyme superoxide dismutase (SOD), which is an enzymatic antioxidant and functions to inactivate and terminate free oxygen radicals (Heryani et al., 2011). When the generation of free radicals exceeds the concentration of antioxidants, oxidative stress will arise.

Exposure to air freshener for 30 days can certainly increase free radical activity so that over time it triggers chronic inflammation. In the process, there is tissue destruction regulated by inflammatory cells, edema accompanied by inflammatory infiltrates including macrophages, lymphocytes, and plasma cells, as well as repairs involving proliferation of new blood vessels and fibrosis. had a thicker septal thickness than the other groups. In the PK1 and PK2 groups, it was shown that giving doses of date palm powder at doses of 120 mg/kgBW and 240 mg/kgBW were not effective in improving the appearance of alveolar septal thickness in the test group which had been exposed to room deodorizers.

In groups K1 (date powder dose 120 mg/kgBB), K2 (date powder dose 240 mg/kgBB), and K3 (date powder dose 360 mg/kgBB) had significant differences compared to group P and septal thickness which was not so different from K0 group. This is because date palm powder is a plant that is potentially safe, effective, and has important medicinal value (El-Morsi et al., 2014) so it does not have a negative effect on septal thickness. As is well known, date pollen contains phenolic compounds as potent antioxidants and will inhibit the formation of free radicals. 16,5 In different organs, the administration of date powder doses has also been studied by Bahmanpour et al., (2006) where date palm powder doses of 120 and 240 mg/kgBB has a good effect on increasing cell function. It can be concluded that giving date palm powder at this dose does not cause damage to the histology of the interalveolar septum and can protect the lungs from oxidative damage.

Whereas in the PK3 group (fragrance and date powder dose 360 mg/kgBB), this group had a significantly different and thinner interalveolar septal thickness than group P. This explained that the higher dose of date powder had the best antioxidant effect in the test group. which has been exposed to air freshener.

Exposure to air freshener for 30 days containing formaldehyde can trigger an oxidative stress response and an inflammatory process. After being exposed to air freshener, the test animals were given date powder according to the dose. There have been many studies investigated that date powder contains antioxidants such as flavonoids, alkaloids and carotenoids (Abedi, A., Parviz, M., Karimian, S.M., Sadeghipour Rodsari, 2012); (Bahmanpour et al., 2006); (Dostal et al., 1996); (Yakubu et al., 2008). Antioxidants will neutralize free radicals before they attack other cells so that they can minimize cell damage. giving a dose of 360 mg/kgBB can affect the thickness of the interalveolar septum because there is extra antiapoptotic activity due to the greater amount of antioxidants. Exposure to formaldehyde causes histopathological changes in the rat lungs and plays an oxidative role for respiratory structures including the lungs whereas date palm powder is able to reduce histopathological changes and protect the lungs from oxidative damage.

According to Rautiainen et al., (2016) the antioxidant activity of phenolic compounds can be said to be comparable to standard antioxidants, such as vitamin C, vitamin E, and b-carotene. In addition, it was also found that the flavonol fraction isolated from dates increased the removal of cholesterol from macrophages. This antioxidant effect can protect cell membranes from being oxidized by the effects of free radicals that are generated extra and intracellular (Borochov-Neori et al., 2015). Antioxidants as free radical neutralizers make them harmless to other cells. can reduce oxidative damage to DNA bases in humans (Kotepui, 2016) and protect cells from lipid peroxidation (Basu et al., 2014).

The presence of the aromatic ring of the flavonoid molecule allows the donation and acceptance of electrons from free radical species so that it has antioxidant properties that help prevent oxidation damage to cells, lipids and DNA. Flavonoid content plays an important role in promoting antioxidant activity, cell health, normal tissue growth, and renewal throughout the body (Dolas Ashadevi & Gotmare, 2015). Flavonoid compounds have been shown to have many benefits, namely as antioxidants, anti-carcinogenic, antimicrobial, antimutagenic, and anti-inflammatory (Al-Farsi & Lee, 2008).

Changes in alveolar diameter are influenced by the mechanism of edema and the presence of atelectasis. This condition is triggered by exposure to air fresheners containing formaldehyde. The P group (perfume) had the smallest alveolar diameter compared to the other seven groups and had a significantly different diameter compared to the K0 group (control). There is an increase in cellularity in the alveolar walls due to the proliferation of alveolar cells causing thickening alveolar septum in white rat histology.

With an increasingly thickened septum, compression occurs in the interalveolar space and narrows the diameter of the alveoli. Exposure to air freshener causes a chronic inflammatory process, which can be continued with tissue fibrosis and then atelectasis or shrinkage of the alveolar walls so that they cannot fill with air (collapse). This process will further narrow the diameter of the

alveoli. Inflammatory and fibrotic processes can trigger septal thickening and suppress the interalveolar space, then narrow the diameter of the alvoelus.

In group K1 (date powder dose 120 mg/kgBB), K2 (date powder dose 240 mg/kgBB), and K3 (date powder dose 360 mg/kgBB) were significantly different from group P which showed that date palm powder did not give any histological changes. worse for alveolar diameter. It is well known that date palm powder has effective antioxidant and anti-inflammatory properties. Dates powder can also effectively boost the immune system to fight toxicity.

The PK3 group (perfume and dates dose of 360 mg/kgBB) had the widest diameter compared to the PK1 group (perfume and dates dose of 120 mg/kgBB) and PK2 (perfume and dates dose of 240 mg/kgBB). There was a significant difference between the P and PK3 groups so that it could be interpreted that the administration of date palm powder at a dose of 360 mg/kg BW was effective in producing the best alveolar diameter picture. This condition is caused by reduced apoptotic processes in tissues due to more antioxidant activity. The more antioxidant activity, the less damage to tissue components (Mahaldashtian et al., 2016), where the tissue damage arises from exposure to air freshener for 30 days. The content in this air freshener can trigger thickening of the interalveolar septum and narrowing of the alveolar diameter. Continuous exposure can trigger an inflammatory process as well as increased free radical activity. Let's return to recall that the phenolic compounds contained in date pollen have potent antioxidant functions. Antioxidants can balance the activity of free radicals before they become too active or unstable.

Exposure to formaldehyde causes a disruption in the physiological balance of oxidant and antioxidant enzymes in lung tissue and triggers lung inflammation. As a protective response to eliminate the cause of injury to cells, the body will remove necrotic tissue and dead cells caused by the damage. Normally any inflammatory process is followed by a repair process to replace damaged cell components. Signs of inflammation will be seen from the response of circulating plasma cells and proteins, extracellular matrix cells, vascular wall cells, and connective tissue around inflammation. Then the inflammatory response will end when the noxious stimulus or inflammatory mediators are gone

Based on the time, inflammation is divided into acute and chronic inflammation. Acute inflammation lasts a short time (a few minutes or a few days) whereas chronic inflammation lasts longer (up to years). The hallmark of acute inflammation is that there is an exudate fluid filled with plasma proteins and collections of neutrophils. Meanwhile, macrophage cells, lymphocytes, vascular proliferation, and scar tissue formation indicate chronic inflammation.

In this study the number of lymphocyte cells increased significantly in group P (fragrances), PK1 (fragrances and dates at a dose of 120 mg/kgBB), and PK2 (fragrances and dates at a dose of 240 mg/kgBB) when compared to group K0 (control). Whereas in the PK3 group (fragrances and a date dose of 360 mg/kg BW) there was a significant decrease in lymphocytes compared to the P group and had values that were not significantly different from the K0 group, although slightly higher. This condition showed a marked increase in lung tissue and a decrease in lymphocyte cells was shown by rat tissue treated with date palm powder after being exposed to formaldehyde. These data indicate that date powder may be an anti-inflammatory agent and date powder can cause a significant reduction in the

production of pro-inflammatory cytokines (Elberry et al., 2011). These results are in accordance with the study of Nady et al (2014) where there was a significant increase in the number of lymphocyte cells for the group exposed to incense smoke. compared to the control group. Then in the study also found a decrease in the number of lymphocyte cells in the group treated with date palm powder. This lymphocyte accumulation constitutes a large number of infiltrating inflammatory cells, which causes loss of orientation and normal alveolar structure as some of the airways and sacs are closed.

As for the number of neutrophil cells, there was a significant increase in the P group when compared to the K0 group. This is not in accordance with the research of Nady et al (2014) where the number of neutrophils in the control group was higher compared to the negative control group and the date powder therapy group. According to Lino et al (2006), exposure to formaldehyde increases leukocyte infiltration into the lungs (increased number of mononuclear cells and neutrophils). Neuropeptides mediate neutrophil accumulation in the lung in a manner regulated by mast cells so that the sequence of events that ultimately leads to formaldehyde-induced lung inflammation could be as follows: formaldehyde stimulus activation of sensory nerve endings neuropeptide release mast cell activation mediator release neutrophil influx. Then this can also be caused by the process of apoptosis which regulates the extent of the inflammatory response and the process of resolution. Inflammatory mediators such as interferon alpha, interleukins 2 and 6, leukotrienes can inhibit neutrophil apoptosis, thereby prolonging neutrophil survival and strengthening lung inflammation. So, it can be hypothesized that this increase in the number of neutrophils, in the end, became a reflex of long survival caused by exposure to formaldehyde (Leal et al., 2018). Whereas in the fragrance treatment group together with date powder, namely PK1, PK2, and PK3, there was a decrease in cell significant neutrophils when compared to the P group.

The decrease in the number of neutrophil cells can be caused by date powder which may act as an anti-inflammatory agent resulting in apoptosis of immune cells during the fight against foreign materials as a result of exposure to formaldehyde when phagocytosis of fine particles occurs as the main defense mechanism.

Whereas in the comparison of the number of macrophage cells, there was a significant increase in the PK3 group when compared to the K0 group. The increase in the number of macrophage cells in the group given date powder treatment was in accordance with the study of Nady et al (2014) where the group exposed to incense smoke and then treated with date powder had more monocytes than the control group. Alveolar macrophages or dust cells are blood monocytes that are found in the connective tissue of the lungs and alveoli. Its main function is to clean the alveoli from inhaled particles and microorganisms. As a defense element, macrophages will phagocytose cell debris, abnormal extracellular matrix, and bacteria that enter the lungs. Normally, dust cells are found in the connective tissue barrier with cytoplasm that contains dust, carbon particles, or other particles that contain dust being digested (Eroschenko, 2003). Increased leukocytosis and increased number of alveolar macrophages are the result of protection against toxic substances inhaled by the body, in this study especially the inhalation of formaldehyde contained in air freshener.

For eosinophil inflammatory cells, the PK1, PK2, and PK3 groups had more cells than the K0 group, although not significantly. This is in accordance with the

study of Nady et al (2014) where the number of eosinophil cells in the group treated with date palm powder after being exposed to incense smoke increased compared to the control group. This could be due to air pollution and microbes that can activate Innate Lymphoid Type 2 (ILC2) in an antigen-independent way. Activated ILC2 releases IL4, IL5 and IL-13, causing non-allergic eosinophilic airway inflammation.

From the results of the study, group C had a number of inflammatory cells. According to Mohamed (2012), histology of the lungs in the control group showed the architecture of the lung tissue, namely clear patent bronchial tubes, alveolar cavities, alveolar sacs, alveolar ducts, and alveoli (picture of two alveoli in one). The thin alveolar walls are lined by two types of type I and type II pneumocytes. The interalveolar septum has normal thickness without abnormalities in the capillaries, normal bronchiolar epithelial architecture was also found and normal aggregation of parabronchiolar lymphoid. and eosinophils in the control group. The normal histology of the alveolar walls mainly contains type I squamous alveolar cells and type II round alveolar cells, alveolar macrophages containing dust or carbon particles in their cytoplasm, very thin-walled capillaries with erythrocytes and leukocytes. The lung tissue of the control group represents normal lung architecture with normal alveoli also lined with simple squamous epithelium.

CONCLUSION

Provision of date powder (Phoenix dactylifera) has an effect on the pulmonary histology of white rats (Rattus norvegicus) exposed to air freshener.The treatment of male white rats (Rattus norvegicus) Wistar strain took place at night because the test animals were nocturnal animals.

It is necessary to carry out further analysis of the harmful chemical substances contained in room deodorizers other than formaldehyde, especially the harmful effects of these substances on the body's respiratory system. The importance of raising public awareness about the harmful effects of using air fresheners containing chemical substances (such as formaldehyde). The public can replace air fresheners that contain chemicals with natural air fresheners

BIBLIOGRAPHY

Abedi, A., Parviz, M., Karimian, S.M., Sadeghipour Rodsari, H. R. (2012). The effect of aqueous extract of Phoenix dactylifera pollen grain on sexual behavior of male rats. *Journal of Physiology and Pharmacology Advances*, *2*(6), 235–242.

Al-Farsi, M. A., & Lee, C. Y. (2008). Optimization of phenolics and dietary fibre extraction from date seeds. *Food Chemistry*, *108*(3), 977–985. https://doi.org/10.1016/j.foodchem.2007.12.009.

ATSDR. (1999). *Toxicological Profile For Formaldehyde*. https://www.atsdr.cdc.gov/toxprofiles/tp111.pdf.

Bahmanpour, S., Panjeh, S. M. R., Talaei, T., Vojdani, Z., Poust, P. A., Zareei, S., & Ghaemian, M. (2006). *Effect of Phoenix dactylifera pollen on sperm parameters and reproductive system of adult male rats*. Iranian Journal of Medical Sciences (IJMS).

Basu, S., De, D., Dev Khanna, H., & Kumar, A. (2014). Lipid peroxidation, DNA damage and total antioxidant status in neonatal hyperbilirubinemia. *Journal of Perinatology*, *34*(7), 519–523. https://doi.org/10.1038/jp.2014.45.

Borochov-Neori, H., Judeinstein, S., Greenberg, A., Volkova, N., Rosenblat, M., & Aviram, M. (2015). Antioxidant and antiatherogenic properties of phenolic acid and flavonol fractions of fruits of 'Amari'and 'Hallawi'date (Phoenix dactylifera L.) varieties. *Journal of Agricultural and Food Chemistry*, *63*(12), 3189–3195. https://doi.org/10.1021/jf506094r.

Dolas Ashadevi, S., & Gotmare, S. R. (2015). The Health Benefits And Risks Of Antioxidants. *Pharmacophore*, *6*(1), 25–30.

Dostal, L. A., Faber, C. K., & Zandee, J. (1996). Sperm motion parameters in vas deferens and cauda epididymal rat sperm. *Reproductive Toxicology*, *10*(3), 231–235. https://doi.org/10.1016/0890-6238(96)00027-5.

El-Morsi, E. M., Abdel-Rahman, M., Ezz, A., & Elhabit, O. (2014). *Study on the Biochemical Effect of Date Palm Pollen on Mice Exposed to Incense Smoke*.

Elberry, A. A., Mufti, S. T., Al-Maghrabi, J. A., Abdel-Sattar, E. A., Ashour, O. M., Ghareib, S. A., & Mosli, H. A. (2011). Anti-inflammatory and antiproliferative activities of date palm pollen (Phoenix dactylifera) on experimentally-induced atypical prostatic hyperplasia in rats. *Journal of Inflammation*, *8*, 1–13. https://doi.org/10.1186/1476-9255-8-40.

Eroschenko, V. P. (2003). *Atlas histologi di fiore dengan korelasi fungsional*. Jakarta: EGC.

Heryani, L., Susari, N. N. W., Kardena, I. M., & Laksmi, D. (2011). Paparan formalin menghambat proses spermatogenesis pada mencit. *Jurnal Veteriner*, *12*(3), 214–220.

Jeleńska, M., Górka-Kostrubiec, B., Werner, T., Kądziałko-Hofmokl, M., Szczepaniak-Wnuk, I., Gonet, T., & Szwarczewski, P. (2017). Evaluation of indoor/outdoor urban air pollution by magnetic, chemical and microscopic studies. *Atmospheric Pollution Research*, *8*(4), 754–766. https://doi.org/10.1016/j.apr.2017.01.006.

Junqueira, L. C., Carneiro, J., & Kelley, R. O. (1995). *Histologi dasar edisi 8*. Jakarta: EGC.

Kotepui, M. (2016). Diet and risk of breast cancer. *Contemporary Oncology/Współczesna Onkologia*, *20*(1), 13–19. https://doi.org/10.5114/wo.2014.40560

Leal, M. P., Brochetti, R. A., Ignácio, A., Câmara, N. O. S., da Palma, R. K., de Oliveira, L. V. F., da Silva, D. de F. T., & Lino-dos-Santos-Franco, A. (2018). Effects of formaldehyde exposure on the development of pulmonary fibrosis induced by bleomycin in mice. *Toxicology Reports*, *5*, 512–520. https://doi.org/10.1016/j.toxrep.2018.03.016.

Lino-dos-Santos-Franco, A., Correa-Costa, M., dos Santos Durão, A. C. C., de Oliveira, A. P. L., Breithaupt-Faloppa, A. C., de Almeida Bertoni, J., Oliveira-Filho, R. M., Câmara, N. O. S., Marcourakis, T., & Tavares-de-Lima, W. (2011). Formaldehyde induces lung inflammation by an oxidant and antioxidant enzymes mediated mechanism in the lung tissue.

Toxicology Letters, *207*(3), 278–285. https://doi.org/10.1016/j.toxlet.2011.09.026.

Mahaldashtian, M., Naghdi, M., Ghorbanian, M. T., Makoolati, Z., Movahedin, M., & Mohamadi, S. M. (2016). In vitro effects of date palm (Phoenix dactylifera L.) pollen on colonization of neonate mouse spermatogonial stem cells. *Journal of Ethnopharmacology*, *186*, 362–368. https://doi.org/10.1016/j.jep.2016.04.013.

Mohamed, A. M. T. (2012). Anatomical and histological effects of formaldehyde inhalation on the lung of albino rat Asmaa Mohamed Tolba Mohamed1, Mamdouh El-Ashtokhy, Hanan Mohamed Ahmed 2, Osama Yasein Ibrahim 3 Human Anatomy and Embryology1, Clinical Toxicology and Forensic2, His. *Journal of American Science*, *8*(9), 395–404.

Mohamed, R. M. A., Fageer, A. S. M., Eltayeb, M. M., & Mohamed Ahmed, I. A. (2014). Chemical composition, antioxidant capacity, and mineral extractability of S udanese date palm (P hoenix dactylifera L.) fruits. *Food Science & Nutrition*, *2*(5), 478–489. https://doi.org/10.1002/fsn3.123.

Spiru, P., & Simona, P. L. (2017). A review on interactions between energy performance of the buildings, outdoor air pollution and the indoor air quality. *Energy Procedia*, *128*, 179–186. https://doi.org/10.1016/j.egypro.2017.09.039.

Tang, Z., Shi, L., & Aleid, S. M. (2013). Date fruit: chemical composition, nutritional and medicinal values, products. *Journal of the Science of Food and Agriculture*, *93*(10), 2351–2361. https://doi.org/10.1002/jsfa.6154.

Türkoğlu, A. Ö., Sarsılmaz, M., Çolakoğlu, N., Zararsız, İ., Kuloğlu, T., Pekmez, H., & Taş, U. (2008). Formaldehyde-induced damage in lungs and effects of caffeic acid phenethyl ester: a light microscopic study. *European Journal of General Medicine*, *5*(3), 152–156.

Yakubu, M. T., Akanji, M. A., Oladiji, A. T., & Adesokan, A. A. (2008). Androgenic potentials of aqueous extract of Massularia acuminata (G. Don) Bullock ex Hoyl. stem in male Wistar rats. *Journal of Ethnopharmacology*, *118*(3), 508–513. https://doi.org/10.1016/j.jep.2008.05.020.