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Mitigative role of red palm on oxidative and antioxidant levels following exposure to mosquito coil smoke in female Wistar rats

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Abstract

Female infertility, which results in disruption of the female reproductive function has link to indiscriminate or chronic burning of Mosquito coil (MC) culminating in increased levels of oxidative stress biomarkers. Oils with significant antioxidant effects have shown promising attenuating effects on oxidative stress processes in reproductive function. The study investigates the mitigative role of red-palm oil (RPO) on oxidative and antioxidant activities following exposure to mosquito coil smoke in female Wistar rats. The study employed 60 female rats of 160-200 grams and was randomly place into 5 groups. Group A was exposed to environmental air only, group B received 2ml of red-palm oil only, groups C was exposed to mosquito coil for 2-hours, groups D exposed to 4-hours of mosquito coil smoke and group E was treated with 2 ml of red-palm oil and 4-hours of mosquito coil smoke for 21-days. Data obtained was analysed using Graph pad prism 9.5 using ANOVA followed by post-Hoc Turkey comparison, and alpha was set at $p \leq 0.05$. Rats exposed to MC resulted in a significant increase in MDA levels, significant decrease in SOD, CAT, and GSH levels in exposed groups C and D compared to A. Treatment with RPO significantly reduced the levels of MDA in groups B and E as compared to D. Conversely, SOD and GSH showed a significant increase levels following RPO in groups B and E compared to D; and CAT had no significant difference in treatment groups B and E following RPO intake. Thus, the study concludes that RPO has an ameliorative effect by mitigating the effect of lipid peroxidation of MC exposed rats.

Keywords: Female infertility; Mosquito coil; Red-palm oil; Oxidative stress; Antioxidant; MDA level; Superoxide dismutase; Catalase; Glutathione reductase

1. Introduction

Female reproductive function is directly determined by the ovarian life span. One of the dominant mechanisms subserving ovarian aging is oxidative stress induced by the accumulation reactive oxygen species (ROS) levels (1); hence precocious ovarian aging can possibly ensue when ROS levels remain perpetually high and continually overwhelming the natural antioxidant systems in female. Ovary is a metabolically active organ and serves as a germ cell reservoir during reproductive life span of female. It consists approximately 0.3 million primordial follicles that contain diplotenearrested oocytes (2,3). Superoxide dismutase (SOD), Catalase (CAT), and reduced glutathione (GSH) are considered to be the most important endogenous enzymes in protecting oxidative challenged tissues as they exhibit synergistic interactions by protecting each other from specific free radical attacks (4,5). Superoxide dismutase is a protective enzyme that can selectively scavenge the superoxide anion radical by catalyzing its dismutation to hydrogen peroxide (6,7). Catalase breaks down hydrogen peroxide (H_2O_2) to water and molecular oxygen while GPx reduces H_2O_2 to water at the cost of oxidation of reduced glutathione (GSH) (8).

Oxidative stress may induce reproductive dysfunction and infertility (9). It has been well demonstrated that oxidative stress affects oocyte integrity by disruption of the spindle structure (10), premature primordial follicle activation (11), antral follicle destruction and impairing the oocyte fusibility (11), deficit of mitochondria-derived ATP (12) and

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induction of postovulatory oocyte aging (13). Mosquito coil (MC) is a slow-burning structure made mainly of insecticides along with inert materials such as wood floor, coconut shell powder, and starch (14) used in repelling mosquitoes (15). It releases several air pollutants and toxic compounds upon burning, to prevent the mosquitoes bite (14); however, it is air pollutant in indoor environment and prolong exposure to the smoke is detrimental to human health (16)(Idowu *et al*., 2013). Although fumes generated upon burning these coils help repel mosquito bites, it has been found that burning a single mosquito coil has the same negative effect as burning 75–137 cigarettes, in addition to the emission of formaldehyde that is equivalent to 51 cigarettes (17,18).

Mosquito coil, when burnt releases not only pyrethrin/pyrethroids, but also carbon monoxide (CO), fine particles (particulate matter < 2.5 microm in diameter; PM(2.5)), polycyclic aromatic hydrocarbons (PAHs), and ketones, volatile organic compounds (VOCs), sub-micrometer particles (PM1), volatile, semi-volatile organic compounds, carbonyls species such as formaldehyde, benzene and acetaldehyde, and gaseous pollutants such as nitrogen oxides, xylene, sulfur dioxide (15,19–23). This results in degenerative changes, inflammation, hemorrhage, induce oxidative stress in the liver, testes, kidney, heart, brain, lungs, leading to a decrease in the number of healthy eggs, cell death in the ovaries (24–29). Further, Madhubabu and Yenugu (30) reported that MC smoke induces elevated levels of reactive oxygen species (ROS) and overexpression of the stress-responsive gene p53. Oxidative stress (OS) (DNA damage-mediated)-induced up regulation of p53 is considered a critical and early event of mitochondria-mediated apoptosis (31).

Red Palm oil (RPO), one of the most widely consumed cooking oils in the tropics, is obtained from the mesocarp (pulp) of the fruit of the oil palm (*Elaeis guineensis*). The oil is consumed fresh (red) or refined at various levels of oxidation. RPO was one of the most preferred remedy for several illnesses in many African countries (32). It consists of a balanced fatty acid composition of about 50 % saturated, 40 % monounsaturated and 10 % polyunsaturated fatty acid content. Consumption of fresh palm oil has been found to generate certain beneficial physiological and biochemical functions contributing to a decline in cardiovascular disease (CVD), kidney disease, liver disease and lung disease. Palm oil extract has been proven economically and biologically important (33). Also, RPO has been demonstrated by various researchers to be nutritionally healthy while establishing a correlation of consumption of palm oil with several health beneficial properties such as toxin reduction, vitamin A source and antioxidant (34). Reports have shown that RPO contains antioxidants, micronutrients such as α- or β-carotene, tocopherols, tocotrienols, phytosterols, squalene and coenzyme Q10 including carotenoid, vitamin K, Coenzyme Q10, squalene, phytosterols, flavonoids, phenolic acids, and glycolipids (35–37). Thus, this antioxidants indicated in the RPO have been found to be effective against oxidative stress both in *vitro* and *in vivo* (38,39).

Therefore, it could be postulated that MC smoke induces apoptosis-mediated tissue damage in subjects with prolonged exposure (Abdulla Al-Mamun *et al*., 2017). The objective of the present study is to examine the effects of inhaling mosquito coil smoke on the antioxidant and oxidant biomarkers in the ovaries of female Wistar rats and the ameliorating effect of red palm oil.

2. Materials and methods

2.1. Mosquito coil

Esbiothrine 0.1%w/w and Transfluthrine 0.05%w/w, manufactured by Gongoni Company Limited Nigeria), was purchased from a super market in Nnewi, Anambra State.

2.2. Experimental animals

A total of 60 female adult Wistar rats weighing 160-200 grams were obtained from the Animal House, Department of Human Physiology, Faculty of Basic Medical Sciences, College of Health Sciences, Nnamdi Azikiwe University, Nnewi Campus. Animals kept in standard cages at room temperature of 27±2 °C; rats were fed with standard pellets and given water *ad libitum*. The rats were randomly divided into five groups of twelve (12) rats each.

2.3. Ethical approval

This was obtained from the Animal Ethics Committee, Nnamdi Azikiwe University, Awka. Rats handling and treatments conformed to Helsinki's Declaration.

2.4. Animal grouping

Sixty-(60) adult female Wistar rats was used at this stage of the experiment; the rats were grouped into five (5) groups of twelve female Wistar rats each (n = 12) labeled as groups A, B, C, D and E.

- Group A: This served as the control group and were only be exposed to environmental air
- Group B: received Red Palm oil only at a dose of 2ml daily for 3 weeks orally using an oral cannula
- Group C: exposed to mosquito coil smoke in an inhalation chamber for 2 hours daily for 3 weeks
- Group D: exposed to mosquito coil smoke in an inhalation chamber for 4 hours daily for 3 weeks
- Group E: exposed to mosquito coil smoke in an inhalation chamber for 4 hours daily and administered 2ml of palm oil one daily for 3 weeks orally using oral cannula.

Vaginal cytology was done on the last day of exposure to know the estrus phase of each rat and ensure even selection of rats that are of the same estrus phase.

2.5. Inhalation chamber

This was locally constructed with the dimension 2.0 x 0.98 x 1.55 m (40)(Method of Mshelia *et al*., 2013).

2.6. Inclusion criteria

Vaginal cytology: Collecting Vaginal Cells (Vaginal Lavage) as described by McLean et al. (41) was done on the last day to know the estrus phase of the rats. Only rats in dietrus and estrus phases were sacrificed and utilized for oxidative stress makers.

2.7. Preparation of tissue (ovary) homogenate for oxidative stress and antioxidant biomarkers (Method of Iftikhar, 2022)

The abdominal cavities of the rats were carefully opened, the ovaries identified and excised, washed using washing solution (11.5g of KCl dissolved in 1,000ml of distilled water). These were homogenized using a homogenizer in phosphate buffer (pH 7.4) (1.98g of K_2HPO_4 and 3.89g of KH_2PO_4 in 400ml of distilled water). The homogenates were centrifuged using a refrigerated table centrifuge at 10,000 net grams for 10 minutes at 4^oC to remove large particles and the supernatants used for Lipid peroxidation, SOD, Catalase and GSH determination (42).

2.8. Determination of oxidative stress parameters

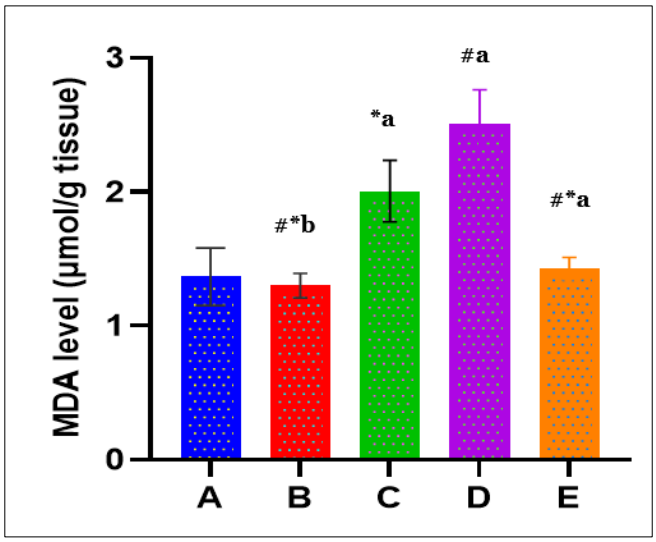
Oxidative stress parameters was determined in the ovaries by using standard methods. Lipid peroxidation was determined by the method of Varshney and Kale (43). The activity of SOD was assayed using the method of Misra and Fridovich (44). The method reported by Aebi (45) was adopted for the assay of catalase activity. The reduced glutathione concentration was estimated using the method of Ellman (46).

2.9. Statistical Analysis

Data obtained from this study was analyzed using Graph pad prism 9.5. Data obtained for MDA, SOD, Catalase, reduced glutathione (GSH) was analyzed using One-way Analysis of Variance (ANOVA) followed by Post-hoc Fisher's Least Square Difference (LSD) to test for level of significance. The results were expressed as Mean ± Standard Error of Mean (SEM). Values of $p \leq 0.05$ were considered statistically significant.

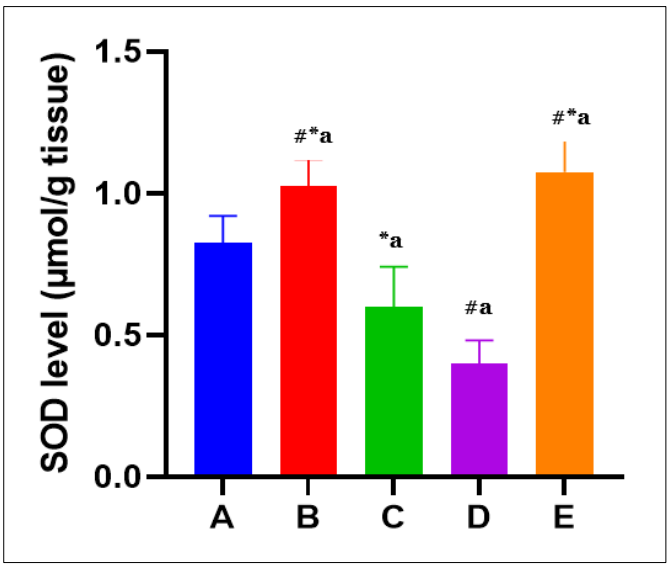
3. Results

Fig 1 shows the MDA result had a significant increase in groups C and D while groups B and E had no significant difference when compared to group A, but had a decrease in groups B and E. Comparison to group C showed a significant decrease in groups B and E, group D had a significant increase. Groups B, C, and E had a significant lower MDA levels when compared to group D.



SEM: standard error of mean, a: significant compared to A, #: significant when compared to C, *: significant compared to group D, and b, c, and d: not significant compared to A, C, and D.

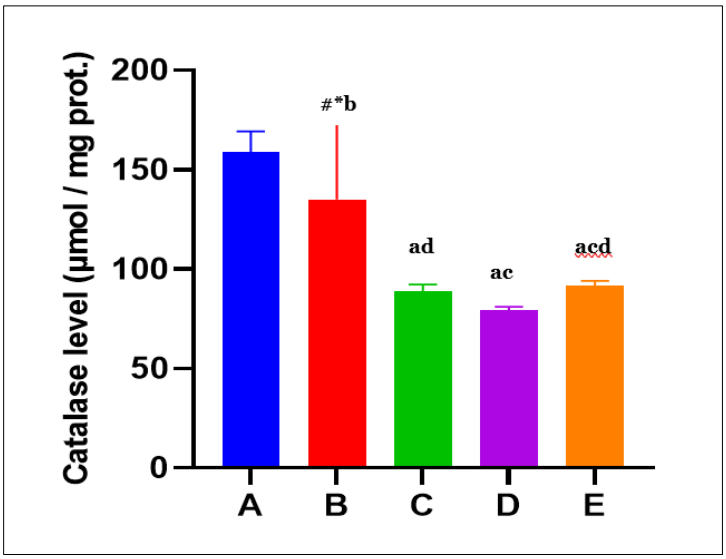
Figure 1 Effect of mosquito coil smoke inhalation and oral administration of palm oil (2ml) for 21 days on lipid peroxidation in the ovary of female Wistar rats



SEM: standard error of mean, a: significant compared to A, #: significant when compared to C, *: significant compared to group D, and b, c, and d: not significant compared to A, C, and D.

Figure 2 Effect of mosquito coil smoke inhalation and oral administration of palm oil (2ml) for 21 days on SOD in the ovary of female Wistar rats

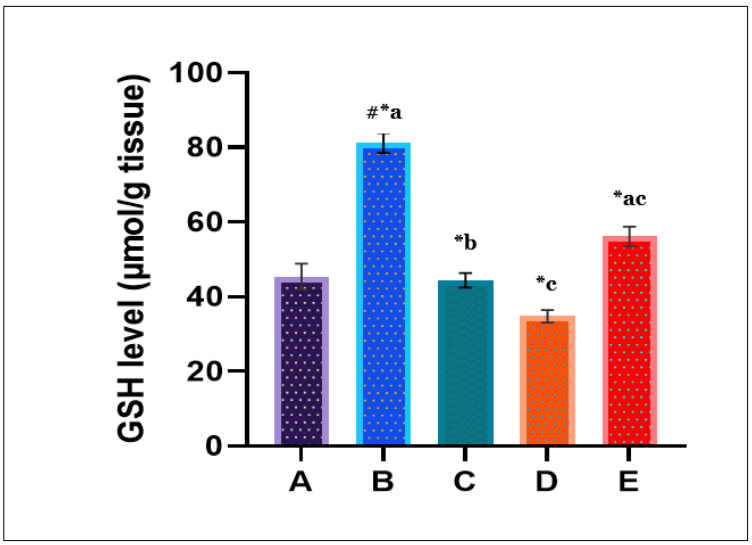
The SOD level result showed a significant difference in groups B, C, D, and E when compared to group A, but groups B and E had an increase while groups C and D had a decrease. Comparison to group C indicated a significant increase in groups B and E while group D had a significant decrease. Groups B, C, and E had a significant increase when compared to group D.



SEM: standard error of mean, a: significant compared to A, #: significant when compared to C, *: significant compared to group D, and b, c, and d: not significant compared to A, C, and D.

Figure 3 Effect of mosquito coil smoke inhalation and oral administration of palm oil (2ml) for 21 days on activity of catalase in the ovary of female Wistar rats

The result of the mean catalase showed a significant decrease in groups C, D, and E while group B had no significant decrease when compared to group A. Groups D and E had no significant difference compared to group C while group B had a significant increase. However, groups C and E had no significant difference while group B had a significant increase compared to group D.



SEM: standard error of mean, a: significant compared to A, #: significant when compared to C, *: significant compared to group D, and b, c, and d: not significant compared to A, C, and D

Figure 4 Effect of mosquito-coil smoke inhalation and oral administration of palm oil (2ml) for 21 days on the activity of GSH in the ovary of female Wistar rats

The GSH result revealed a significant increase in the mean levels in groups B and E, while group D had a significant decrease and group C had no significant change when compared to group A. Comparison to C showed a significant difference in group B and D, while group E had no significance, however, group B had an increase and D had a decrease. Groups B, C, and E had a significant increase when compared to group D.

4. Discussion

Oxidative stress can have detrimental effects on female fertility by affecting ovulation, fertilization, embryo development, and implantation. OS impacts fertilization and can further induce apoptosis, resulting in embryo fragmentation, implantation failure, or abortion (47). Semiquinone radicals present in fine particles ($PM_{2.5}$), undergo redox cycling as a result causes oxygen reduction leading to generation of reactive oxygen species (ROS) (48). Also, exposure to combustion products such as polycyclic aromatic hydrocarbons (PAHs) have been associated with increased oxidative stress biomarkers (49,50) as metabolites of PAH having electrophilic properties covalently attaches to intracellular macromolecules, leading to the generation of ROS (51). The ovaries being one of the organs with polyunsaturated fatty acids are prone to oxidative stress assaults by oxidants. The study investigates the mitigative roles red palm oil on lipid peroxidative markers and antioxidants following mosquito coil toxicity in ovary of Wistar rats.

The study showed that MDA result had a significant increase in groups C and D while groups B and E had no significant difference when compared to group A. Also, Comparison to group C showed a significant decrease in groups B and E, group D had a significant increase. Groups B, C, and E had a significant lower MDA levels when compared to group D. The physiology linked to the significant increase in the MDA level is generation of free oxygen radicals, which has shown to cytotoxic effects by causing peroxidation of membrane phospholipids, which results in an increase in membrane permeability, loss of membrane integrity, enzyme inactivation, structural damage to DNA and cell death (52,53). Higher concentrations and accumulation of the enzyme malondialdehyde not only damages the cells but also triggers the process of apoptosis (54). The works of (15,55–58) showed similarity to the study findings revealing an increased lipid peroxidation of experimental rats to mosquito repellants. However, the study demonstrated that administration of mosquito coil post-treatment with red palm oil, established an improved levels of MDA, which was reduced significantly. The mechanism of action following the significant reduction of MDA levels is linked to scavenging effects on ROS levels in the ovarian tissue, which is demonstrated by palmitic acid, oleic acid, vitamins C and E respectively. However, these phytonutrients and micronutrients have shown to inhibit the excess hydroxyl radicals and nitrogen radicals generated in the ovarian tissue by inhalation of MC by scavenging these ROS production through complex pathway.

The study findings showed a significant decrease in groups C and D following MC exposure in the ovarian SOD level compared to group A. However, the physiology following the decreased levels of SOD activities in the ovarian tissue is caused by increased lipid peroxidation, which is indicated by increased hydroxyl radicals and nitrogen species generated. However, the depleted level of SOD is attributed to the depletion of Cu, Zn and Mn which are important cofactors for SOD, hence suggested reproductive toxicities associated with MC exposure in experimental models. The works of Ayeleso *et al*., (59) and Ikechukwu *et al*. (60) reported significant increased levels of SOD activities, which disagree with the study findings. The report of Jewo *et al*. (61) showed significantly lower levels of SOD following mosquito coil exposure in the male rats, which agrees to the study report. Also, treatments with RPO against MC exposure in experimental rats and alone, revealed a significant increase in the levels of ovarian SOD as indicated in groups B and E when compared to group D. Further, the mechanism associated with the significant higher ovarian SOD levels following RPO is the presence of vitamin C and E as well as palmitic and oleic acids, which tends to combat ROS formation. The study report shows similarity to the work of Oguntibeju *et al.* (33) reported a statistical significant increase in the activities of SOD in rat erythrocytes following dietary supplementation with red palm oil. Conversely, Katengua-Thamahane (62) report is similar to the study findings, indicating that administration of RPO supplementation significantly increased mitochondrial SOD2 protein expression levels in the myocardial cells of spontaneously hypertensive rats and that the possible mechanisms underlying RPO-induced salutary effect could be via modulation of the nitric oxide/cyclic guanosine monophosphate (NO-cGMP) signalling pathway. RPO has ability to modulate the oxidative sensitive mitogen-activated protein kinase (MAPK) signaling pathways.

The study showed that exposure to MC in experimental rats demonstrated a a significant decrease in groups C, D, and E while group B had no significant decrease when compared to group A. The significant decrease in catalase level of the ovary shows the increased level of ROS production as indicated by the increase MDA activities; this agrees with previous studies by Dauqan *et al*. (63) and Ikechukwu *et al*. (60) using the liver of Wistar rats. Also, the stud showed consistencies with works of Sachan, (64); Odukanmi *et al*. (65); Scalios (66) revealing a significant decrease in Catalase activities. However, treatments with RPO as indicated in-group E revealed a significant increase in the activity of catalase when compared group D. This implies that, palm oil exerted a salutary effect on catalase suppressing action of mosquito coil smoke. This corroborates findings by Nwaogu *et al*. (67), Sunmonu and Oloyede (68); that red palm oil enhances activities of catalase.

Twenty-one (21) days oral administration of palm oil (5ml) caused a statistically significant increase in the activity of GSH in the ovaries at $p \leq 0.001$ when compared with the control, this agrees with Ayeleso *et al*., (2013); they reported

that, palm oil increases glutathione activities in the liver and blood of male Wistar rats. Exposure to mosquito coil smoke for two (2) hours per day and four (4) hours per day for twenty-one-(21) days caused a statistically significant decrease in the activity of GSH in the ovaries when compared with the control. The physiology linked to decreased activities of GSH is formation of excess hydroxyl radicals, which tends to cause depletion of the antioxidant systems of the ovarian tissue. Oyeniran *et al*. (69) showed similar findings following exposure to MC, which resulted in a significant decline in serum GSH levels. Also, this study findings corroborates the reports of Kurawa *et al*. (15), Fetoui, and Gdoura, (70). Exposure to mosquito coil smoke for four (4) hours followed by an oral administration of palm oil (2ml) daily for twenty (21) days caused an increase in the activity of GSH when compared with the negative control (mosquito coil 4 hours exposed group) though not significant at $p \leq 0.001$. The reason for the significant rise in the GSH following RPO is linked to the present of micronutrients (Vitamin C and E), which are exogenous antioxidants that scavenges excess ROS in tissues. A study by Achuba and Nwokogba, (71) showed that, palm oil enhanced GSH activities in organ/tissues of rats subjected to oxidative stress, which corroborated findings by Okpoghono *et al*. (72) who reported that, plant derived materials attenuated oxidative stress induced in rats fed with crude oil contaminated diet by enhancing reduced glutathione activity (72).

5. Conclusion

The study revealed that mosquito coil exposure resulted in lipid peroxidation in ovarian tissue, which caused a depletion in the antioxidant levels, resulting to apoptosis. However, treatment with red palm oil improved the lipid peroxidation and antioxidant status of the ovarian tissue. Thus, red palm oil could be used an antioxidant in managing oxidative stress level following mosquito coil exposure in both experimental and human studies.

Compliance with ethical standards

Disclosure of conflict of interest

There was no conflict of interest between the authors.

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Contributions made among the authors

Eje drafted the manuscript and did the biochemical assays, Eyeghre and Eje did the statistical analysis, and Prof. Maduka and Eyeghre edited the drafted manuscript.

Statement of ethical approval

An ethical approval was obtained for the study on the use of female Wistar rats according to the conformity of the guidelines of Faculty of Basic Medical Sciences, Nnamdi Azikiwe University, Nnewi Campus with the ethical number given as NAU/CHS/NC/FBMS/714.

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