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EFFECT OF GREEN TEA EXTRACT (CAMELLIA SINENSIS) ON MDA LEVELS OF WHITE RAT (RATTUS NORVEGICUS) OVARY EXPOSED TO MSG (MONOSODIUM GLUTAMATE): A LITERATURE REVIEW

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ABSTRACT

This literature review aims to determine the effect of green tea extract on ovarian MDA levels exposed to MSG in white rats. The journals studied in this literature review are 10 journals published in 2010-2020 and discuss the effect of exposure to MSG on rat ovaries and treated with antioxidants (Green Tea, Vit C&E, etc.). Results: Of the 10 journals studied, there were 5 journals which said that giving MSG exposure to female rats would increase ovarian and uterine MDA levels. In 5 other journals the results showed that MSG exposure could cause hypertrophy, atrophy, degenerative changes, and changes in the diameter of the follicles, as well as changes in ovarian histology. Exposure to antioxidants (green tea, vitamin C and vitamin E, aloe vera, chorella vulgaris and spirulina plaatensis) shows good results for repairing histological changes in the ovaries and serves to prevent increased levels of MDA in ovaries that have been exposed to MSG because antioxidants are effective in reducing oxidative effects. Stress from MSG exposure in rats that have been exposed to MSG.

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Keywords: MSG (Monosodium Glutamate), MDA (Malondialdehyde), Ovary, Green Tea, Mice.

INTRODUCTION

Fertility is one of the skills possessed by a woman in producing offspring. This skill is often associated with the fertile period of women. The results of 2017 Indonesian Demographic and Health Survey (SDKI) from the National Population and Family Planning Agency (BKKBN) show that the infertility rate increased by around 0.2 children (Prawirohardjo, 2011). This increase in infertility can be caused by various factors, including nutritional/food factors. Consumption of fast food types with various kinds of flavor enhancers that use chemicals, one of which is widely known as Monosodium Glutamate or micin (Hanum et al., 2020). Monosodium Glutamate, or MSG, is a salt compound usually used as a food flavoring in everyday life. MSG is a regulator of cell movement and Gonadotropin Releasing Hormone (GnRH) in the body. Consumption of MSG in the United States is 0.5 g/day. In Taiwan, it is three g/day, while in Indonesia, it is an average of 0.6 g/day. The maximum limit for using MSG is 120 mg/kg/day. When MSG levels in the body are excessive, it can increase the amount of glutamate in the blood plasma, triggering free radicals which cause cell death. The death of these cells will later affect all body organs contaminated with glutamate, especially causing malfunctions in the female reproductive organs. One way to detect damage to cell organs due to MSG is to detect lipid peroxidation levels with the help of Malondialdehyde (Hamza & Diab, 2020).

Malondialdehyde (MDA) is a product of synthesis in the body from the process of lipid peroxidation. The high or low concentration of MDA in the body indicates an oxidation process in the cell membrane, also

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known as oxidative stress. One of the functions of MDA is that it can measure lipid peroxidation levels stably and accurately and can serve as a detection agent for most diseases originating from excess oxidative stress (Menzel et al., 2021).

Oxidative stress can increase free radicals that trigger various diseases in the body. However, one solution that can reduce this radicalization is with the help of endogenous antioxidants. Endogenous antioxidants produced in the body are the natural protectors of the human body from free radicals, which cause disease to enter the body quickly. Even though the human body already has endogenous antioxidants, their effectiveness will decrease when the body's radicalization is higher. For this reason, other types of antioxidants are needed to help excess radicalization in the human body in the form of exogenous antioxidants (Tondy et al., 2021). Various natural ingredients have many antioxidants. One of the easiest to find and most potent antioxidants is the herbal plant green tea (Camellia Sinensis). Green tea, in nature, is rich in polyphenols, theophylline (0.03-0.05%), organic acids (1.61%), lignin (5.9%), free amino acids (1.1-5.6%)), caffeine (3.51%), theobromine (0.16-0.21%), and theanine (5%) (Greening et al., 2015).

There are four classifications of substance content in green tea—first, phenolic compounds, non-phenolic compounds, aromatic compounds, and enzymes. Phenol content is dominated by polyphenols or flavonoids, which function as body protectors against free radicals. Next is the catechins. Catechins are potential compounds in the formation of exogenous antioxidants which act as antioxidant suppliers to overcome oxidative stress effects (Mason et al., 2020). Besides that, catechins are also promising antioxidant compounds and are easily absorbed by the digestive organs of the human body. The content of catechins in tea has a higher level of antioxidant activity than vitamins C and E (Intra & Kuo, 2007). Based on the above review, the researcher is interested in conducting a literature review regarding the Effect of Green Tea Extract (Camellia Sinensis) on MDA Levels of White Rat (Rattus Norvegicus) Ovary Exposed to MSG (Monosodium Glutamate). This study aimed to determine the association of green tea extract in preventing increased ovarian MDA levels in white rats (Rattus norvegicus) exposed to excessive MSG (Monosodium Glutamate).

METHOD

The research design is in the form of library research or literature review (literature review). A literature review aims to identify, assess and interpret research results from a research topic so that a solution is obtained to answer the planned research question (Kitchenham et al., 2011). The research review used is the effect of green tea extract on ovarian MDA levels. Mice exposed to MSG.

The dependent variable is the change in ovarian MDA levels after being given MSG and green tea, and the independent variable is exposure to MSG. This study's sample used ten journals explaining MSG and green tea exposure to ovarian changes and MDA. The sample inclusion criteria used in this study include: 1) journals are national and international journals with a full publication year of 10 years; 2) journals using Indonesian and English; 3) international journals obtained from the website are reputable journals; 4) national journals that are published with a minimum accreditation of sinta – 5; 5) journals are available in full text and original journals; 6) Journals with keywords: Green tea, antioxidants, MDA, ovaries, and monosodium glutamate (MSG).

The research article search strategy was carried out using the keywords: green tea extract, antioxidants, polyphenols, catechins, MDA, ovaries, MSG. in several databases such as google scholar, science direct, PubMed, Springer, ProQuest, Scopus, and research gate. This literature review was carried out from August 2021 to May 2022. Initially, 50 journals were obtained from databases that were relevant to the topic. Then a screening was carried out so that the remaining 38 journals were carried out. A feasibility assessment was carried out, and the results obtained were ten feasible journals following this study's inclusion criteria.

RESULT AND DISCUSSION

Study Characteristics

Ten studies met the inclusion criteria according to the literature review topic, namely the effect of green tea extract on the ovarian MDA levels of white rats exposed to MSG. Seven journals that discuss the effects of antioxidants (Green Tea, Vitamin C, and Vitamin E, Aloe Vera, Chorella Vulgaris, and Spirulina Plaatensis) are related to the title of the literature review. There are four journals related to MSG exposure to the ovaries, namely the number of follicles, follicle diameter, and histological changes in the ovaries. There are four journals and one journal related to the uterus and MDA. At the same time, five journals discuss MSG exposure to ovarian MDA. On average, these studies were conducted in Asian countries, with one study in Pakistan, one in India, four in Indonesia, two in Nigeria, and two in Egypt. The research design of the ten journals used in this literature review is an experimental study.

Characteristics of Study Population/Sample

The samples in the ten journals used in the Literature Review are, on average, using healthy female rats aged 2 to 3 months and weighing 100 – 250 grams. The study is an average of around 14-40 days.

Intervention Method

Given MSG exposure to female rats, almost all journals were administered orally. Giving MSG exposure is mixed with 1 – 1.5 ml of distilled water. On exposure to antioxidants, the average is given orally. They are giving antioxidants given after 2 hours. They are giving MSG. The dose for each antioxidant is different because the plants used to produce antioxidants are also different.

Data Synthesis Results

Overall, from the ten journals used in the literature review, five journals said that giving MSG exposure to female rats would increase ovarian and uterine MDA levels. In 5 other journals, the results showed that MSG exposure could cause hypertrophy, atrophy, degenerative changes, changes in the diameter of the follicles, and changes in ovarian histology. Exposure to antioxidants such as green tea, vitamin C and vitamin E, aloe vera, chlorella Vulgaris, and spirulina plaatensis show promising results for repairing histological changes in the ovary and can also prevent an increase in MDA levels in ovaries that have been exposed to MSG because antioxidants are effective in reducing the effects of oxidative stress. MSG exposure in rats that have been exposed to MSG.

Effect of MSG Exposure on Ovarian MDA Levels

The four literature reviews reviewed show that exposure to Monosodium Glutamate (MSG) can affect the increase in Ovary MDA levels (Kamalah et al., (2019); Kayode et al., (2020); Rohmawati, (2016); Rohmawati et al. ., (2014). These results follow previous studies, which showed that exposure to MSG affected increasing Ovary MDA levels. The results of the data synthesis found that the lowest MSG exposure was in rats, with a dose of 0.71 mg/gbb/day. 0.71 mg/gbb/day shows an increase in ovarian MDA levels caused by oxidative stress. Oxidative stress will later damage organs infected with excess glutamates, such as the hypothalamus. In addition, oxidative stress also causes organ damage in the ovary, especially regarding its histological structure (Sayuti & Yesrina, 2015). Laurence et al. (2008) stated in their research on co Inversion that the dose of rats weighing ~ 201 g against human body weight is 70 kg, which is 56, so the dose given to rats will be multiplied by 56. If converted from a rat dose of 0.7 mg/grBW/day to a human dose, the conversion results are known, namely s7.84 gr. So, a human with a body weight of 70 kg and consumes MSG more than or equal to 7.84 grams per day in the long term can allow the effect of exposure to MSG, which will harm the body and increase ovarian MDA levels caused by oxidative stress that affects the reproductive system. The Food Drug Administration (FDA) stated that the limit for consumption of MSG in humans with a body weight of 70 kg is 120 mg/KgBb or 9.6 g/day (Rachma & Saptawati, 2021).

According to Abdulghani et al., (2022), MSG administration can show an increase in Ovary MDA levels in female rats. Besides that, the MSG administration also shortens the period in the diestrus, proestrus, and estrus phases. The impact of giving excess MSG is also the cause of cell degeneration in the granulosa and degeneration in the ovum. The impact that occurs can also cause a decrease in ovarian follicles as a whole, both secondary and tertiary follicles. In

addition, the impact of excess MSG also causes a decrease in the corpus luteum and an increase in the number of atretic follicles. According to Kesherwani et al., (2022), exposure to MSG can increase MDA levels in the plasma due to free radicals, so increased MDA levels indicate an increase in oxidative stress. According to Pereira et al., (2022), the increase in radicalization that occurs in the human body is caused by a decrease in the level of activation of antioxidant enzymes and an increase in the content of malondialdehyde (MDA) in plasma. However, in the journal, Khaled et al., (2022), which is against the theory, say that exposure to MSG can reduce Ovary MDA levels due to free radicals. In addition, MSG also interferes with ovarian function in female rats by increasing the secretion of LH and FSH hormones from the anterior pituitary and estradiol from the ovaries, and increases oxidative defense, follicular maturation, and impairs uterine function by stimulating estradiol sensitivity to oxytocin and inhibiting progesterone sensitivity to oxytocin. Therefore, the relationship between the dose and the duration of MSG exposure to the decrease in MDA levels and the effect on the hypothalamus should be further studied because there is the possibility of different research results which are thought to be caused by the different doses of exposure and the time of exposure to MSG.

The increase in Ovary MDA levels is due to the presence of free radicals. Free radicals appear when consuming excess MSG resulting in high glutamate levels in blood plasma, triggering natural biological processes involving pro-oxidants ROS (reactive oxygen stress) and RNS (reactive nitrogen stress). Free radicals are caused by the presence of free electrons that do not have a partner, so they try to approach other electrons that are nearby. Free deradicalization is usually referred to as oxidation, giving rise to new free radical molecules. ROS formation is considered the first cause due to oxidative stress. Therefore, high levels of glutamate can cause damage to cell organs. This damage then attacks other organ cells that have other glutamates, causing all organs to be exposed. Damage to internal organs due to glutamate can provoke the appearance of free radicals, which react with fat, protein, and cellular nucleic acids. This reaction then triggers excessive damage that causes specific organs to fail to function, such as the ovaries. One of the causes of oxidative stress is high levels of MDA in the ovaries (Al-Shahat et al., 2022; Ibrahim et al., 2021; Khashchenko et al., 2020; Xue et al., 2022).

The production of reactive oxygen species (ROS) can be related to PUFA (Poly Unsaturated Fatty Acid), which is the cause of lipid peroxidation, one of the results of MDA. Similar results were also said by Aboubakr et al., (2021) that increased levels of MDA and decreased endogenous antioxidants were caused by CAT (catalase), SOD, and GSH. Increasing the composition of glutamate in plasma will have an impact on the central nervous system resulting in the formation of ROS. ROS then becomes a catalyst for oxidative stress, which triggers increased lipid peroxidation in the body, causing organ damage. The two lipid peroxidation types often used in research on oxidative stress are isoprostanes (IsoPs) and MDA.

The Effect of Giving Green Tea on Ovary MDA Levels Exposed to MSG

The way to reduce the destructive effects of excess MSG is to use exogenous antioxidants. When the human body cannot anticipate oxidative stress using endogenous antioxidants, other antioxidants are needed in the form of exogenous antioxidants, which can be obtained through green tea extraction. Green tea is a compound with high levels of exogenous antioxidants that can inhibit the rate of ROS, hydroxyl, peroxyl, and superoxide anion radicals through its content called catechins (Sayuti et al., 2020). Three journals used in this literature review discuss the antioxidant content of the green tea plant (Camellia Sinensis) (Bharti & Singh, 2020; Jakubczyk et al., 2020; Kochman et al., 2020). Green tea (Camellia Sinensis) was given to experimental animals in the form of green tea extraction, which functions as an antioxidant and can minimize the impact of oxidative stress. The three journals above said the same results, namely an increase in Reactive Oxygen Species (ROS) and MDA, as well as a decrease in antioxidant enzymes, namely superoxide dismutase (SOD), catalase (CAT), and glutathione (GSH) which are indications of oxidative stress. In addition, the three journals also said that there were different histological depictions of the ovary in the form of cell hypertrophy, degeneration, and atrophy of the granulosa cell layer. This can be overcome by giving antioxidants contained in green tea.

This follows the theory from Fawzeh et al. (2019), which said that giving MSG to experimental animals can reduce the activity of antioxidant enzymes such as glutathione peroxidase (GPx) and superoxide dismutase (SOD). Superoxide dismutase (SOD) catalyzes the redox conversion of superoxide radicals to hydrogen peroxide and oxygen. Glutathione peroxidase (GPx) catalyzes the reduction of hydrogen peroxide by two GSH molecules. Furthermore, there was a significant increase in MDA levels and a decrease in the activity of superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx) given MSG. However, when given green tea extract, it showed a decrease in MDA levels and increased antioxidant enzyme activity. These results can be confirmed by Szulińska et al. (2017) in their research on the form of extracting green tea, which has many positive effects through its various antioxidant contents.

According to the theory, antioxidants can reduce ROS activation in the body's system (Hashim et al., 2011). The content of green tea in the form of Flavonoids functions as an antidote to various free radicals. The process of reducing free radicalization using Flavonoid scavenging is carried out by giving hydrogen or electron functional groups to Flavonoid and RH free radicals. Flavonoid radicals have a slower activation tendency than most free radicals. Furthermore, flavonoid radicals also tend to bind to radicals, becoming non-reactive compounds (Sandhar et al., 2011). Based on research conducted by Procházková (2011), Flavonoids can minimize the effects that occur due to free radicals through their bond to ROS. Then flavonoids can also easily reactivate antioxidant enzymes and metal chelating. They can overcome a-tocopheryl radicalization, which causes obstacles in the oxidation process and mitigation of nitric oxide reactions.

The polyphenol content in green tea can reactivate antioxidants, which are more accessible and higher than vitamins C and E. In addition, the polyphenol content in green tea can protect cell membranes due to ROS and other pathologies. Polyphenols that have been obtained through green tea extraction are believed to be able to minimize the development of dioxide (O2-), hydroxyl (OH), and peroxyl radicals (ROO). Besides that, polyphenols also can minimize the growth of ROS in all cell organelle membranes in body compartments that occur due to damage due to oxidative stress. The polyphenols in green tea are rich in carotenoids, tocophenols, ascorbic acid, phytochemicals, and various minerals such as Cr, Mn, Se, and Zn, which function as antioxidant enhancers (Weanbiao, 2013).

Other plants that contain antioxidants, such as green tea, include vitamins C and E. In this literature review, two journals discuss the effect of antioxidant content, which is better than vitamins C and E, on the MDA of ovaries exposed to MSG (Laili et al., 2015; Saygin et al., 2018). The journal showed that the antioxidant activity in administering a combination of vitamins C and E could inhibit ovarian toxicity caused by MSG treatment by reducing oxidative stress and reducing ovarian MDA levels. This is also in line with other studies which say that Vitamin C has a protective effect that can help improve ovarian histology that has been exposed to MSG, the reason being that vitamin C protects the capillary endothelium from oxidative damage by increasing the synthesis of nitric oxide, collagen, and extracellular matrix (Amiri-Rigi & Abbasi, 2016).

Apart from green tea and vitamins C & E, aloe vera, chlorella Vulgaris, and spirulina plaatensis plants contain antioxidants. The journals used in this literature review show that aloe vera can minimize the harmful effects of MSG and has a positive effect by increasing the diameter of secondary and mature Graafian follicles (Joshi et al., 2021). de Oliveira et al., (2019) also said that aloe vera leaf extract could reduce lipid peroxidase levels and increase the effectiveness of glutathione peroxidase (GPx, catalase (CAT), and reductase. Collecting free radicals in aloe vera can benefit changes in pathologically produced ROS. Chlorella Vulgaris and spirulina plaatensis also say that they can increase the activity of superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx) and can also alleviate ovarian dysfunction that has been exposed to MSG (Aziem et al., 2018).

CONCLUSSION

The result of converting rat doses into human doses is around 7.84 g/day. If consumed for a long time, it can harm the body and increase

ovarian MDA levels caused by oxidative stress, which affects the reproductive system. How neutralize it by providing antioxidants (green tea, vitamins C & E, aloe vera, and Chorella Vulgaris and spirulina plaatensis) can prevent an increase in ovarian MDA levels that have been given MSG exposure and improve ovarian dysfunction. This happens because antioxidants can reduce oxidative stress caused by MSG.

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