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The Use of Spices and Fruit as Marinades to Prevent and Reduce HAA (Heterocyclic Amines Aromatic) and PAH (Polycyclic Aromatic Hydrocarbons) Levels in Grilled or Fried Meat to Prevent Cancer

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ABSTRACT

Cancer is a deadly non-communicable disease, and one of the contributing factors to the increased risk of cancer is the consumption of carcinogenic compounds such as heterocyclic aromatic amines (HAAs) and polycyclic aromatic hydrocarbons (PAHs) during high-temperature cooking processes, as well as some oxidative reactions that can increase the risk of cancer. This scoping review aims to analyze articles discussing spices and fruits that can reduce the carcinogenic compounds Heterocyclic Amines and Polycyclic Aromatic Hydrocarbons to prevent cancer in animal protein sources (meat, fish, and their processed products). A total of 2,400 studies were identified during the database search. After excluding studies that did not meet the inclusion and exclusion criteria, 3 studies were obtained. Since the search with these criteria yielded few results, a snowballing technique was adopted to search for studies, resulting in 76 studies found through backward searching and 62 studies found through forward searching. After excluding studies that did not meet the inclusion and exclusion criteria, 5 studies were found through backward searching and 2 studies were found through forward searching, with a total of 10 studies obtained. This research states that marinating with natural spices can effectively reduce the levels of carcinogenic compounds in grilled or fried meat products. Although the acquired results show considerable potential, there remains a requirement for additional studies into the precise processes of these active chemicals and their long-term impacts on human health.

Keywords: Cancer, PAHs, HAAs, Carcinogenic, Marinade, Spices, Fruit, Antioxidant

INTRODUCTION

The disease of cancer is one of the deadliest non-communicable diseases. According to the World Health Organization, it was the second greatest cause of death before the age of 70 in 112 of 183 nations in 2019, ranking third or fourth in 23 countries. The Global Cancer Observatory reports that there are 18.1 million new cases found every year, with the potential to increase the annual death toll to 9.6 million¹. Cancer affects 1.4% of the population in Indonesia, with the province of DIY (Special Region of Yogyakarta) experiencing the highest rate at 4.1%, markedly exceeding the national average. In 2013, both breast and cervical cancers were the most prevalent types in Indonesia, with breast cancer accounting for 0.5% and cervical cancer for 0.8%².

Consumption of carcinogenic substances, such as heterocyclic aromatic amines (HAAs) and polycyclic aromatic hydrocarbons (PAHs), is one factor that can lead to an increased risk of cancer. The Maillard reaction and the Strecker degradation of precursors such as amino acids, creatinine, and glucose result in the production of toxic substances known as HAAs and PAHs when meat and processed meals are cooked over elevated temperatures³. The generation or prevention of HAAs production is influenced by the antioxidants used during processing, ion type, precursor quantity, meat amino acid type, and meat pH⁵. Moreover, the appropriate addition of sugar can also reduce the formation of carcinogenic compounds⁶. Antioxidant compounds can be found in spices and fruits, which can reduce the formation of carcinogenic compounds.

Several researches have shown that spices and fruits have the potential to suppress the production of HAAs and PAHs due to their high antioxidant content. For example, a latest study found that coriander root extract (CRE) can inhibit the formation of PAH8 by 87.4% and coriander leaf extract (CLE) can inhibit the formation of PAH8 by 51.8%⁷. Dry apple peels, green tea, olive oil, beer or red wine, rosemary, garlic, onion, red chilli, paprika, ginger, turmeric, and black pepper are examples of antioxidants found in spices and fruits that can prevent the production of HAAs by acquiring pyrazine cation radicals or carbon-centered radicals in both chemical models and cooked meat^{29,30,14}. However, these studies are still limited, and only a few provide a comprehensive overview of the effectiveness of other natural ingredients in reducing carcinogenic compounds. Therefore, a systematic review is needed to identify the most effective spice ingredients in preventing cancer.

MATERIAL AND METHOD

This scoping review aims to analyze articles discussing spices and fruits that can prevent cancer by lowering the production of carcinogenic substances such as Heterocyclic Amines and Polycyclic Aromatic Hydrocarbons. It also aims to identify areas that require further research. The search strategy and method for finding articles can be seen in Figure 1.

Research Questions

What spices can inhibit and reduce the formation of HAA and PAH?; What fruits can inhibit and reduce the formation of HAA and PAH?; What active compounds contribute to the production of HAA and PAH in spices and fruits that can reduce carcinogenic compounds?

Identification of Relevant Studies

The sources referenced are from online databases such as Google Scholar, PubMed, and ScienceDirect. All referenced articles have been published within the last five years, specifically from 2020 to 2024, and are freely accessible. The materials are available in both Indonesian and English. The types of methods used for this review are experimental and systematic. Due to the limited results obtained from these criteria, the snowballing technique was applied to enhance the search for review materials both forward (by reviewing articles based on citation metrics) and backward (by examining the reference lists of articles)⁸.

Study Selection

The authors selected relevant articles focusing on 1) spices that can reduce the formation of HAA and PAH; 2) fruits that can reduce the formation of HAA and PAH; 3) active compounds that can reduce the formation of HAA and PAH. The keywords used by the authors are "carcinogenic compounds" "Polycyclic Aromatic Hydrocarbons" "Heterocyclic Amines" "Cancer".

Charting Data

There were 2,400 articles were obtained from the systematic search, and 3 articles met the inclusion criteria. The snowballing technique was then applied to find additional articles by checking the references of existing articles and those that cite them. From the

snowballing technique, we obtained 7 articles. So, there are 10 articles that will be used for the scoping review. Then, the authors screened based on the predetermined criteria and identified the research findings related to the effectiveness of these ingredients in reducing Polycyclic Aromatic Hydrocarbons and Heterocyclic Amines carcinogenic compounds.

Object Criteria

1) research on animal-based protein sources (meat and fish) and their derivatives; 2) examination of spices, sugar, and fruits; 3) publication in English language; and 4) accessibility in free full-text only. The excluded article criteria were research on humans and animals, and articles not related to substances that can reduce carcinogenic compounds HAA and PAH.

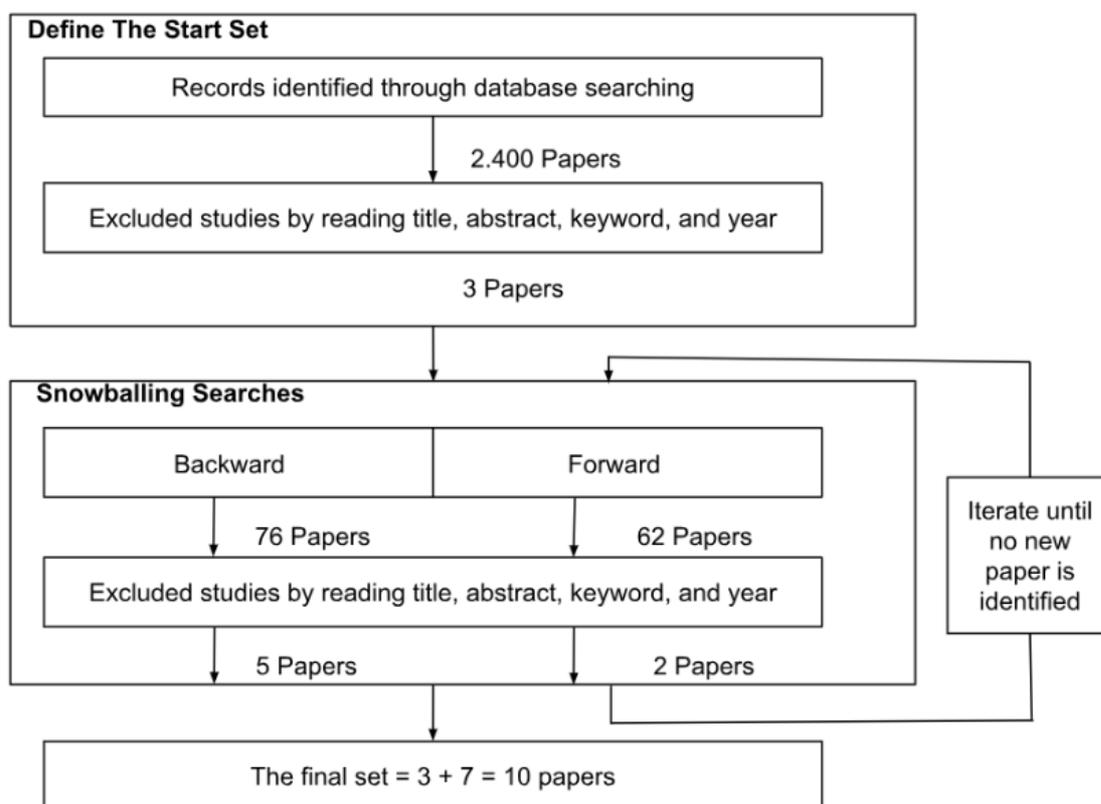


Figure 1. Flow Chart of Scoping Review (Wohlin, 2014)⁹

RESULTS AND DISCUSSION

Table 1. An overview of research spices, sugar, and fruits can reduce HAA dan PAH

No	Country; authors	Type of herb and spices	Research object	Active compound	Method	Result
1	Beijing; Yajie et al., 2022 ⁷	<i>Coriandrum sativum</i> L.	Duck wings	Phenolic	Experiment	Phenolic compounds in coriander root extract can be an effective inhibitor in the formation of carcinogenic PAH compounds in roasted duck wings.

2	Malaysia; Hasyimah et al., 2020 ¹⁶	Honey	Beef	flavonoids and phenolic acids	Experiment	The active compounds flavonoids and phenolic acids, as well as the sugar content (sucrose and fructose) in honey, play a crucial role in reducing the levels of carcinogenic Polycyclic Aromatic Hydrocarbons (PAH) and Heterocyclic Amines (HAA) in meat satay.
3	China; Yao et al., 2020 ¹²	Tea	Chicken	Antioxidant (Aqueous extract of green tea are catechins, quinic acid, caffeoyl glucose, caffeoylquin ic acid, and rutin)	Experiment	The antioxidants in tea can reduce the formation of HCA and BaP by neutralizing free radicals formed during the grilling process. Electric grilling is safer than charcoal grilling.
4	Indonesia; Yunita et al., 2023 ¹³	Lemon juice (<i>Citrus limon</i>)	Chicken	Phenol, Citric Acid	Experiment	Marinating chicken with 15% lemon can reduce Polycyclic Aromatic Hydrocarbons (PAH) as the citric acid in lemon lowers the pH of the chicken and reduces PAH formation. The natural antioxidants in lemon also reduce PAH formation.
5	China; Bao et al., 2020 ¹⁴	Black pepper	Fish (Tilapia)	The Alkaloid Piperine	Experiment	The addition of 1% black pepper to fried tilapia can inhibit the formation of total HAA due to the antioxidant compounds present in black pepper.
6	Saudi; Khan et al., 2020 ¹⁵	Blueberry, raspberry, and strawberry	Camel, beef, and chicken	Antioxidant	Experiment	Marinating with fruit extracts (blueberry, raspberry, and strawberry) for at least 6 hours can reduce the formation of carcinogenic HCA compounds by 40-100%.

7	Taiwan; Hsu and Chen., 2020 ¹⁰	Black pepper, rosemary, red pepper, and soy sauce	Chicken products	Tryptophan, Phenylalanine	Experiment	Rosemary has been proven to be the most effective in inhibiting the formation of HCA and COPs during chicken grilling compared to black pepper and red pepper. However, it has the opposite effect on soy sauce, which can increase HCA formation.
8	Turkey; Kilic et al., 2021 ²²	Turmeric (<i>Curcuma longa</i>)	Chicken meatball	Curcumin	Experiment	A 0.5% addition of turmeric can reduce the risk of HAA exposure in chicken meatballs and enhance the product quality.
9	Korea; Jeong et al., 2023 ²⁴	Paprika (<i>Capsicum annuum</i> L.)	Pork	Carotenoids (Capsanthin and Capsorubin)	Experiment	The addition of sodium nitrite and paprika extract during pork bread storage can inhibit the formation of heterocyclic amines.
10	China; Hu et al., 2021 ²⁵	Garlic and garlic essential oil	Pork sausages	Organosulfur (Allicin (diallylthiosulfinate))	Experiment	The allyl methyl trisulfide (AMTS) found in garlic essential oil (GEO) has the strongest inhibitory effect on BaP formation, reducing BaP levels by 63.3% in pork sausages.

Ten research articles met the inclusion criteria. The conclusions of these ten research articles are shown in Table 1. Based on these ten articles, it was found that heated protein-rich foods such as fish and meat contain heterocyclic amines (HAs)¹⁰. The creation of cancer-causing substances in processed meats and fish is affected by both internal and external factors, which can be reduced through various methods, such as selecting the suitable sugar for marinating, utilizing the correct processing or treatment techniques, and incorporating both synthetic and natural antioxidants into meat and fish⁶.

A recent study reported that peking duck roasted in open-air at 270°C for 40-45 minutes can produce polycyclic aromatic hydrocarbons¹¹. Roasting peking duck in open-air can produce 129 µg/kg of 19 PAH (including PAH8). Numerous natural components, including spices and fruits, have been studied and demonstrated to lower the development of carcinogenic substances like polycyclic aromatic hydrocarbons (PAH) and heterocyclic amines (HAs). Natural antioxidants have demonstrated the ability to decrease the development of carcinogenic substances like PAH and HAA in both meat and fish³. Coriander root extract (CRE) can inhibit the formation of PAH8 by 87.4% and coriander leaf extract (CLE)

can inhibit the formation of PAH8 by 51.8%⁷. Other research also revealed that marinating grilled drumsticks using white tea on wood charcoal burning can reduce HCs by 23.35%¹². Similarly, another study found that the lowest PAH4 levels were found in chicken satay marinated with 15% lemon¹³. Tilapia fillet fried contained 18.73 ng/g of HAAs during 8 minutes of frying, and the level of HAAs decreased when black pepper was added¹⁴. Several research results revealed that marinating with antioxidant-rich ingredients such as garlic and others before processing protein-rich products, meat, and fish can reduce or even inhibit the formation of HAA and PAH^{27, 28}.

Marinating is a non-thermal technology and some components of marinades work against microbes and autooxidation¹⁵. In this study, we summarize marinades that can be used in frying and grilling processes to reduce the risk of cancer caused by carcinogenic substances that arise from the processing process. In a study, researchers used coriander root and leaf extracts as marinades on duck wings⁷. Researchers used 60 duck wings (around 42 ± 3 g each) were brought from SOGOU superstore (Nanjing, China). Coriander leaf and root extract powder were collected coding as coriander leaf extract (CLE) and coriander root extract (CRE) separately. Five groups of concentration of two extracts (200, 400, 600, 800, 1 000 mg/L) were prepared respectively as marinated groups. Five duck wings were taken for each marinated group, control group (marinated in water) and raw group. Marinating conditions that followed the descriptions of Wang et al. were 1:1 (m/V) at 4 °C for 4 h. The findings revealed that coriander root extract (CRE) inhibited PAH production more effectively than coriander leaf extract (CLE). The strongest inhibitory impact was obtained at a concentration of 600 mg/L coriander root extract, which reduced PAHs by 87.4%. In addition, this study discovered a favorable link between PAH production and the level of free radicals in roasted duck wings. Marinades containing phenolic compounds from coriander are effective in lowering the quantity of free radicals that lead to the development of PAHs. In general, phenolic compounds can block free radical chain transfer events by chelating catalytic metal ions or giving hydrogen/electrons to unstable intermediate radicals such as lipid hydroperoxides, which are key in the synthesis of PAHs⁷.

PAHs and HCAs are carcinogenic chemicals that occur when meat is heated, particularly at high temperatures. Recent research has demonstrated that honey-spice marination can prevent the production of polycyclic aromatic hydrocarbons (PAHs) and heterocyclic amines (HCAs) in gas-grilled beef satay¹⁷. The beef utilized was fresh raw beef flesh (10 kg) acquired from local markets in Seri Serdang, Selangor, and chopped into small beef cubes around 0.5 cm thick and 2 cm wide with a clean stainless steel. Honey marination reduces the creation of these toxic chemicals, however at high temperatures, this impact becomes less important because to the pyrolysis reaction that happens in the fat and protein in the meat.

Electric grilling produces the lowest content of HCAs and BaP, while charcoal grilling, especially bamboo charcoal, produces the highest content, especially in carcinogenic compounds such as benzo[a]pyrene. A similar study provided its research results, which showed that white tea marination was the most efficient in lowering the development of HCAs and BaP compared to green tea and oolong tea marination¹². Chicken legs weighing between 90 and 100 g and of comparable size and form were selected for this study. After that, 1% of the drumstick ratio was made up of green, oolong, and white teas, which were put to the heated marinade. Additionally, samples were marinated for 10 hours at 48 °C. White tea helps prevent the production of carcinogenic chemicals by strengthening the body's defenses against free radicals. According to the study, tea's antioxidant content—particularly its polyphenols, such as catechins—is thought to be crucial in halting the production of HCAs and

BaP while grilling. Polyphenols have been shown to boost GSH concentrations and SOD activity in the liver, reduce blood lipid and liver cholesterol levels, and improve the overall potential of the antioxidant system¹⁸.

Lemon marinade, which contains citric acid, has been demonstrated to be beneficial at lowering meat pH, reducing cooking loss, and enhancing the water holding capacity (WHC) of chicken meat, particularly in chicken satay¹³. Chicken satay is made by cutting lean chicken breast flesh lengthwise into thin slices measuring 5 x 2 x 1 cm. Marinade the beef in lemon juice for 15 minutes, using three different concentrations: 15%, 20%, and 25%. The reduction in pH is caused by an interaction between the acid in lemon juice and meat protein, which contributes to increased softness and spice absorption in the meat. Chicken satay marinated in 15% lemon juice has the lowest pH and the highest WHC, indicating that the flesh is softer and juicier. The concentration of lemon juice utilized increases the water content of the meat while decreasing the fat content. The reduction in fat content happens because lemon juice helps break down the fat structure during the grilling process. However, the use of lemon juice has no significant impact on protein levels, which remain stable even though the grilling process can cause protein denaturation at high temperatures because the low pH value in the acidic marinade increases the tenderness of the meat by lowering the pH, which in turn causes the weakening of the muscle structure, and the decrease in meat pH to below the isoelectric point can increase the positive charge of myofibrillar proteins, which causes the expansion of the protein network¹⁶. The study pointed out that organic acids contribute to the degradation and dissolution of connective tissue, resulting in a decrease in the diameter and thickness of muscle fibers, which causes swelling of meat fibers and increased proteolysis by cathepsins (the optimal pH for this activity is 3.5-5.0). The study found that lemon juice greatly reduced the production of carcinogenic PAHs such as benzo[a]pyrene, chrysene, and benzo[b]fluoranthene, particularly in satay marinated with 15% lemon juice. This is due to the antioxidant content of lemon juice, such as vitamin C, polyphenols, and flavonoids, which can fight off free radicals and reduce the development of hazardous chemicals during the grilling process¹³.

Recent research has found that the piperine content of black pepper, which acts as an antioxidant, plays a vital effect in lowering the production of HAAs such as MeIQx and PhIP in tilapia fillet¹⁴. Tilapia fillets will be chopped into 10 g (30 x 30 x 3 mm) pieces and divided into 12 groups based on frying duration (4, 8, and 12 minutes) and black pepper concentration (0, 0.5%, 1.0%, and 1.5%, wt/wt). Piperine inhibits lipid oxidation, one of the primary causes of HAA generation during high-temperature frying. However, the study's findings revealed that low black pepper doses or long frying periods can still cause some forms of HAAs to occur. To reduce the formation of heterocyclic aromatic amines (HAAs) such as MeIQx and PhIP, the use of black pepper at a concentration of 1.0% in the meat marinating process can provide the best results. The recommended marinating time with a mixture of black pepper is 30 minutes before further processing. The study also found that black pepper at a concentration of 1.0% might suppress the development of PhIP and MeIQx by up to 100% in fish fillets fried for 8-12 minutes.

Marinating meat fillets with blueberry, raspberry, and strawberry extracts and 100 mL fruit extract at 4 °C for various time periods (1, 6, 12, and 24 hours) reduced the formation of carcinogenic HCA compounds during cooking¹². This is due to the extract's physical and chemical effects, specifically on the Maillard reaction, which is the primary driver of HCA generation in cooked meat. The extract is able to reduce water evaporation and inhibit the transfer of HCA precursors into the meat. Reducing water loss during cooking is very important because it can affect the distribution and availability of HCA precursors in cooked meat.

Another study explained the antioxidants that play a role in blueberry, raspberry and strawberry extracts, namely phenolic compounds¹⁹. The study examined antioxidant levels using the Ultra-Turrax and Ultrasonic methods with the results of antioxidant levels among the three berries, namely raspberries with the highest ranking, followed by blackberries and the lowest levels are owned by blueberries. They continued that antioxidants in fresh berries are indeed high and even though they have been extracted and become waste, the antioxidant levels in the three berries are still fairly good so that it can be said that the waste antioxidants of the three berries can still be reused. Another study using the ultrasonic-based extraction method on strawberries revealed that antioxidants in fresh strawberries have significant levels².

A total of four raw whole chickens weighing approximately one kilogram were obtained at a local market in Taipei, Taiwan. All four tastes, red pepper, black pepper, rosemary, and soy sauce, were purchased from a local supermarket in Taipei, Taiwan. Grilled chicken seasoned with red chili, black pepper, and rosemary (30 g, 3%; red pepper, black pepper, rosemary) can inhibit the production of COP and certain forms of HA. Chicken skin has a greater total HA content than meat, but total COP varies depending on whether it is grilled in a fan oven or a superheated steam oven, except black pepper¹⁰. Grilled chicken skin is more likely to generate HA, whereas meat is more prone to COP development. The study revealed that chicken skin is more prone to HA creation because it includes more fat and protein, which are significant precursors in HA synthesis when subjected to high heat during grilling. The production of HA begins with the Maillard reaction involving sugar, amino acids, and creatinine, which happens more easily in the fat-rich skin. The greater cholesterol concentration in chicken flesh makes it more vulnerable to COP production. When grilled, cholesterol in meat undergoes oxidation especially if heated for a long time. In one study, researchers stated that rosemary can inhibit the formation of thermally degraded HA¹⁰. Another study found that marinating meat with rosemary and cold-pressed oil significantly increased the phenolic acid content, which helps reduce lipid oxidation during grilling. This antioxidant property is primarily due to the presence of rosmarinic acid, carnosol, and carnosic acid in rosemary, which are known to stabilize lipids in meat, improving texture and flavor while extending shelf life²¹.

The use of turmeric can reduce the levels of heterocyclic aromatic amines at various temperatures tested in recent studies²². This research used chicken breast meat minced with a 3 mm grinding plate which was then divided into three portions (30 g). The group without turmeric served as the control group. In the other two groups, turmeric was added at rates of 0.5 and 1%. Afterwards, the meatballs were stored in the refrigerator (+4 °C) for 4 hours and then formed using a steel mold (the weight of each meatball was approximately 60 g). There are no additional ingredients and/or spices (except turmeric) used in making meatballs. The effectiveness of this reduction depends on the amount of turmeric used, with the best results found in meatballs containing 0.5% turmeric. In addition, turmeric also has a positive effect on reducing weight loss during cooking and lipid oxidation, which are important indicators of meat quality. It is anticipated that adding 0.5% turmeric to chicken meatballs reduces the risk of exposure to carcinogenic HAAs while also improving product quality. Malondialdehyde (MDA) is a major end product of lipid oxidation. In one study, turmeric had a substantial effect, with 1% turmeric containing the lowest MDA component level²³.

The combination of nitrite and paprika extract can reduce protein and lipid oxidation in pork, lowering HCA formation²⁴. Although both are effective, their mechanisms are different, namely sodium nitrite works through the inhibition of oxidation by binding oxygen, while paprika contains carotenoids such as capsanthin and capsorubin which act as scavengers of

free radicals and reactive oxygen. In this study, sodium nitrite, which is commonly used as a preservative in processed meat, has the potential to generate carcinogenic nitrosamine compounds if used in excess, however, sodium nitrite was utilized in a very tiny amount (0.7 mg), which is within the safe limit for intake. Although paprika extract inhibits several types of HCA, in this study several HCAs such as MeIQx and PhIP increased in greater amounts in patties given paprika extract. Therefore, the stability and effects of paprika extract under certain conditions must be considered carefully. The pig patties used in the study were standardized to have an equal round form with a diameter of 90 (± 2) mm and weight of 100 (± 5) g using a petri plate.

Benzo[a]pyrene (BaP) is one of the polycyclic aromatic hydrocarbons (PAH) that is a carcinogenic chemical comprising two or more benzene rings and can be formed by incomplete combustion or pyrolysis of organic materials²⁵. Garlic has sulfide compounds in its essential oils, such as allyl methyl trisulfide (AMTS), diallyl sulfide (DAS) and diallyl disulfide (DADS) which have the ability to inhibit the formation of BaP. The study also explained the mechanism of sulfides in organosulfur in influencing the formation of BaP in the process of grilling pork sausages related to the removal of free radicals. Sulfides with more sulfur bonds are more reactive in capturing free radicals which causes a significant reduction in BaP as evidenced by the results of AMTS showing the highest BaP inhibitory effect (63.3%). The pork sausages used in the study weighed approximately 100 \pm 10 grams each. They were 1.9 cm in diameter and 20 cm in length, with four versions of garlic powder added at concentrations of 0.05%, 0.1%, and 0.15% (w/w), as well as four variations of garlic essential oil (GEO) included at concentrations of 0.002%, 0.004%, and 0.006% (w/w).

CONCLUSION

The study shows that marinating with natural ingredients like coriander, honey, white tea, lemon, black pepper, rosemary, turmeric, and garlic effectively reduces carcinogenic compounds (PAHs, HCAs, BaP) during high-temperature cooking methods like frying and grilling. The beneficial active compounds include antioxidants and phenolics that inhibit lipid oxidation and reduce free radicals. While the findings are promising, further research is needed to understand these compounds' specific mechanisms and long-term health effects.

AUTHORS' CONTRIBUTIONS

Shofa Ananda: Conceptualization, Methodology, Resources, and Writing-Original. **Razan Shabrina Malahati:** Formal Analysis, Data Curation, and Writing-Original. **Almira Sitasari and Tri Siswati:** Final Writing-Review and Editing, Supervision and Project Administration.

DATA AVAILABILITY

No data was used for the research described in the article.

DECLARATION OF COMPETING INTEREST

The authors declare no conflict of interest.

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