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REVIEW ARTICLE

The Antioxidant Activity of Ambon Banana Peel (*Musa paradisiaca AAA*) against Breast Cancer: A Review

Graciella Virginia Irwantoho, Joya Angelica Immanuel, Ashella Loral Lydia Claire, Valeska Refflyn, Aqeela Syakira Sugarda, Ju Won Lee, Junaida Astina*

Department of Food Science and Nutrition, Institut Bio Scientia Internasional Indonesia, Jakarta, Indonesia

**Corresponding author: junaida.astina@gmail.com*

A B S T R A C T

Breast cancer is one of the most prevalent types of cancer in women around the globe, especially those coming from a low-income population like Indonesia. As a preventive measure, consuming balanced diets containing high antioxidant sources is therefore imperative in reducing the risk of breast cancer. Banana peels, for instance, are an undervalued source of antioxidants, which also possess high economic and nutritional values. This review aims to provide systematic information about the bioactive composition of ambon banana peels (*Musa paradisiaca L.* var. sapientum), their antioxidant mechanism on breast cancer, as well as their potential incorporation into food products, such as flour, cookies, and chips. The review was conducted by examining literature from the past 10 years (2013-2023) that fit the inclusion criteria. Based on the collected studies, Ambon banana peel contains high amounts of bioactive compounds, primarily polyphenols, flavonoids, carotenoids, tannins, saponins, and ferulic acid. Even after the peels are converted into processed food products, the antioxidant activity remains high with proper thermal processing conditions. These antioxidant properties of Ambon banana peels provide promising potential for treating breast cancer through various modes of action. However, clinical studies involving humans are still lacking to further emphasize its therapeutic effects.

K E Y W O R D S

Ambon banana, Peel, Antioxidant, Bioactive compounds, Breast cancer

H I G H L I G H T S

- Ambon banana peel is high in antioxidants that can help to prevent breast cancer.
- This review examines the antioxidant contents of Ambon banana peel and their mechanisms on breast cancer.
- This review summarizes potential applications of Ambon banana peel that can be incorporated in food products.

INTRODUCTION

Breast cancer has become the most prevalent type of cancer diagnosed, resulting in the most deaths annually (Bray et al., 2018). In 2020, up to 2.3 million females received a diagnosis of breast cancer, and over 685,000 death cases were reported globally (International Agency for Research on Cancer (IARC), 2022). In Indonesia, there were 65,858 cases of breast cancer in 2020 (16.6%), with more than 20,000 resulting in deaths from the disease (GLOBOCAN, 2022). Worldwide, the prevalence of breast cancer in young women is generally rather low. In industrialized countries, the median age at diagnosis is 68 years old. However, in Indonesia, the median age at diagnosis is 48 years old, including over 5,000 women under the age of 40 who are diagnosed with breast cancer each year (Anwar et al., 2019). Notably, in young Indonesian women, a delayed diagnosis of breast cancer may be caused by low cancer awareness, particularly in those with lower household incomes and educational levels (Solikhah et al., 2019). This notion is further supported by data from Anwar et al. (2019) study, where most women were diagnosed at the later stages of stage III (47.9%) and stage IV (16%) breast cancer.

Increased exogenous antioxidant levels have been demonstrated to inhibit the forms of free radical damage linked to breast cancer development in laboratory and animal studies (National Cancer Institute, 2014). Hence, consuming antioxidant-rich foods is recommended to help alleviate the likelihood of people acquiring cancer or passing away. Among all foods with abundant antioxidants, banana peels are one of the most underutilized commodities (Okolie et al., 2016). In tropical nations like Indonesia, bananas (*Musaceae.sp*.) are an important agricultural product due to their social, economic, and cultural values. In 2023 alone, up to one hundred thousand tons of bananas were produced in Indonesia (Badan Pusat Statistik Indonesia (BPS), 2023). Particularly, the Ambon banana (*Musa paradisiaca*) is one of the banana cultivars that are native to Indonesia and is mainly grown in both tropical and subtropical regions, including Southeast Asia, Northern Australia, Brazil, Mexico, Colombia, and many more (Cao et al., 2018). This triploid *M. paradisiaca* cultivars (AAA) are regarded as essential dessert bananas on a worldwide scale, characterized by their robust performance, hefty symmetrical bunches of huge fruit, notably curved, creamy white flesh, soft and fine textured, and sweet flavour with aromatic notes (Wahyudi et al., 2020; Hapsari & Lestari, 2016). Its peels are highly overlooked and have amassed tonnes of waste, resulting in gasses that upset the natural equilibrium of the air and give off an unpleasant stench. Therefore, transforming banana peel into a valued commodity would generate financial gain for the agriculture sector (Zaini et al., 2022).

Banana peel has significant antioxidant, antibacterial, and anticancer properties and is abundant in dietary fibre and phenolic compounds. By their well-known antioxidant qualities that go beyond the control of oxidative stress, dietary polyphenols have a significant role in preventing degenerative illnesses, including breast cancer and cardiovascular disorders (Rebello et al., 2014). Banana peels hold significant potential for enhancing human health, as evidenced by their potential for pharmaceutical and nutraceutical applications and the potential benefits of banana peel and pulp extracts for cancer prevention in the general population (Zaini et al., 2022; Mondal et al., 2021). Various discoveries have given researchers more understanding of how banana products work and how they protect against degenerative illnesses thanks to their active ingredients. This review aims to provide information regarding the bioactive compounds in ambon banana peel and their antioxidant mechanisms against breast cancer.

MATERIALS AND METHODS

Search strategy

The literature search for the systematic review on the antioxidant activity of ambon banana peel against breast cancer was conducted using the following databases: Google Scholar, MDPI, ScienceDirect, Semantic Scholar, and PubMed. The keywords used for the systematic searches were: ("antioxidants" OR "antioxidant activity" OR "bioactive compounds" OR "phytochemicals"); AND ("banana peel *Musa Paradisiaca L.*" OR "banana peel *Musa Sapientum*" OR "*kulit pisang ambon*"); AND ("breast cancer" OR "ductal carcinoma" OR "tumour"). Furthermore, several keywords were combined to evaluate specific prompts, such as "antioxidants content in *ambon* banana peels," OR "antioxidants on breast cancer," OR "utilization of *ambon* banana peels into food products."

Eligibility criteria

The studies included in this review were screened based on the inclusion and exclusion criteria. The inclusion criteria were studies within the past 10 years (2013–2023), delivered in English and/or Indonesian, in the form of accessible full-text manuscripts including research articles, e-books, review articles, and thesis/dissertation, and focusing on the antioxidants contained in the peel of Ambon banana (*Musa paradisiaca L*. or *Musa AAA*), their stability and bioavailability, and their mechanisms on breast cancer. Information from official authorities, such as the IARC, Central Bureau of Statistics Indonesia, and GLOBOCAN, was also used as supporting references related to statistical measures. Studies that evaluate different banana cultivars and types of cancers were excluded from the study. The discussion of the studies consists of general information about Ambon banana and breast cancer, the antioxidant potential of Ambon banana peel, the antioxidants' mechanisms against breast cancer, and its valorization into food products with high antioxidant content. In terms of the clinical tests, studies conducted on both humans and animals were included in the search. Additionally, references for data used were analyzed based on the title, year of publication, type of banana and antioxidant, and other related discussions correlated to breast cancer. The selected paper was categorized as primary references as the main source of information, whereas secondary references were used as supporting information and included in the discussion. **Figure 1.** illustrates the overall design of the review method for studies that meet the eligibility criteria.

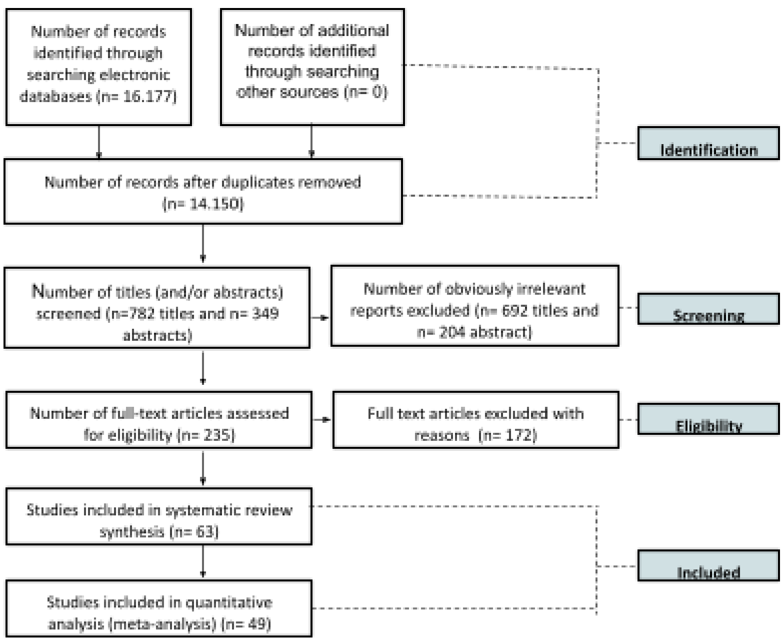

Figure 1. Prisma Flow Diagram

Table 1. Findings of the reviewed sources

Authors	Publication year	Type of source	Aim of study	Relevant Findings/Points
Wardati	2017	Primary	To find the specific IC50 value for banana peel extract against T-47D cells.	● Banana peel extract has moderate cytotoxicity effects on T-47D cells. ● Banana peel shows good potential as a breast cancer chemoprevention agent, particularly effective at high concentrations (>250 µg/mL).
Momenimovahed & Salehiniya	2019	Secondary	To investigate the incidence, mortality rates, and risk factors of breast cancer in the world.	● Breast cancer cases vary depending on race, ethnicity, socioeconomic class, hormonal conditions, hereditary, and lifestyle factors. ● The mortality rate of breast cancer is higher in regions that are less developed.
Dieterich et al.	2014	Secondary	To discuss the key lifestyle factors related to breast cancer and evidence-based prevention strategies for clinical practice.	● Lifestyle modifications in daily habits can reduce the incidences of postmenopausal breast cancer by up to 34%. ● Poor lifestyle factors are linked to a higher risk of breast cancer. ● Women who are overweight or obese may be at a higher risk of developing breast cancer.
Sapudom et al.	2019	Primary	To understand how the mechanical properties of the extracellular matrix are controlled by intrafibrillar crosslinking and how these properties affect breast cancer behaviour.	● Two different breast cancer cell lines, invasive MDA-MB-231 (human breast carcinoma) and non-invasive MCF-7 cells (human breast adenocarcinoma).
Goff &	2021	Secondary	To understand the	● The pathophysiology of

Danford			crucial role of immune cells in normal breast and breast carcinoma in breast cancer prevention and treatment.	breast cancer begins with carcinogenesis, which is driven by external and internal factors. ● These factors can cause changes in DNA sequence and function through protein kinase C activation, subsequently altering cell differentiation. ● Tumor-infiltrating lymphocytes in breast cancer may act as prognostic markers. for chemotherapy response and survival outcomes. ● Immune cells are important throughout the breast carcinogenesis process.
Hikal et al.	2022	Secondary	To understand banana peels' antioxidant and antimicrobial properties, which can serve as valuable natural antioxidants and have potential pharmaceutical applications for treating various diseases.	● Banana peel can be effectively utilized in the food, pharmaceutical, and other industries. ● Banana peel extract contains phenolic compounds, alkaloids, flavonoids, tannins, saponins, glycosides, carotenoids, sterols, triterpenes, and catecholamines, which have been shown to possess antioxidant and antimicrobial activities.
Proverawati et al.	2019	Secondary	To examine the physical and chemical properties of banana peel flour from Plantain, Kapok, and Ambon banana varieties using a completely randomized design.	● Water and crude fibre contents are found to be the highest in Ambon banana peel. ● Ash, fat, protein, and carbohydrates are the highest in Plantain peels. ● The type of banana peel and soaking duration significantly impacted the banana flour's water content, fibre content, and pectin levels.

Rebello et al.	2014	Primary	To investigate the in vitro antioxidant activity of Musa AAA banana peel flour, as well as identify and quantify the phenolic compounds responsible for the activities.	● The high phenolic content in banana peel flour extracts contributes to their significant antioxidant activity, as measured by FRAP (~14 µM/g), ABTS (~242 µM/g), and ORAC (~436 µM/g) in Trolox equivalents. ● Major phenolics include: Highly polymerized proanthocyanidins (~3952 mg/kg as (+)-catechin); Flavonol glycosides (~129 mg/kg as quercetin 3-rutinoside); B-type procyanidin dimers; and monomeric flavan-3-ols (~126 mg/kg as (+)-catechin).
Mondal et al.	2021	Secondary	To provide a comprehensive evaluation of bananas and their phytochemicals for cancer prevention and therapy, emphasizing the cellular and molecular mechanisms of action.	● The bioactive compounds in bananas have demonstrated antiproliferative, cell cycle arrest-inducing, apoptotic, anti-adhesive, anti-invasive, and antiangiogenic effects by modulating various dysregulated oncogenic signalling pathways. ● Banana products and phytoconstituents are essential for the future development of cancer prevention and therapy drugs.
Alamsyah et al.	2016	Primary	To evaluate the antioxidant activity of banana peel extract and watermelon rind extract, as well as their combinations, including in lotion form.	● The antioxidant activity test of the extract revealed that the inhibitory concentration 50% (IC50) value for banana peel is 64.03 parts per million (ppm).
Prakash et al.	2017	Primary	To evaluate the phytochemical and antifungal activity of	● Phytochemical analysis revealed that the banana peel varieties contained

			ripe banana peels.	carbohydrates, phenols, terpenoids, and saponins in both powder and ash form.
Aly et al.	2024	Secondary	To explore recent innovations in plant triterpenoids and their underlying mechanisms of action in fighting breast cancer.	● Triterpenoids significantly inhibit proliferation, migration, and resistance to apoptosis in breast cancer cells, as well as reduce tumor angiogenesis and metastasis. ● The anticancer impact of triterpenoids is linked to their antiproliferative activity, disruption of angiogenesis and cell differentiation, regulation of apoptosis, inhibition of DNA polymerase, alteration of signal transduction pathways, and prevention of metastasis, hence serving as a promising anticancer agent.
Fidrianny & Insanu	2014	Primary	To evaluate the antioxidant capacity of various banana peel extracts using ABTS and DPPH methods, as well as to correlate the total phenolic, flavonoid, and carotenoid content with their antioxidant capacities.	● The ethyl acetate extract of Ambon banana peels exhibited the highest ABTS scavenging capacity, with an IC50 of 1.91 ppm.
Pereira & Maraschin	2015	Secondary	To assess the phytochemical properties and biological activities of *Musa spp* fruit pulp and peel.	● Banana peels contain bioactive compounds: anthocyanins, alkaloids, and phlobatannins. ● Their biological potential is linked to their chemical composition. ● Uses include: provitamin A supplementation, antioxidant properties

				due to phenolic constituents, and treatment of Parkinson's disease.
Corona et al.	2015	Primary	To explore the use of enzymatic reactions and analytical techniques to analyze banana peels and their derived compounds.	• Ferulic acid with an abundance of 0.38% was found in the peel extract of Musa paradisiaca L. using ultra-performance liquid chromatography with electrospray ionization.
Zduńska et al.	2018	Secondary	To investigate the antioxidant properties of ferulic acid and its possible applications.	• Ferulic acid not only acts as a free radical scavenger but also inhibits enzymes that produce free radicals and enhances the activity of scavenger enzymes.
Kumar et al.	2013	Secondary	To discuss the structural characteristics of flavonoids, their health benefits, and their microbial production.	• The bioavailability, metabolism, and biological activity of flavonoids are influenced by their configuration, the total number of hydroxyl groups, and the substitution of functional groups in relation to their core structure. • Many flavonoids are known for their antioxidative properties, free radical scavenging ability, coronary heart disease prevention, hepatoprotective effects, and anti-inflammatory and anticancer activities, with some also showing potential antiviral effects.
Behiry et al.	2019	Primary	To investigate the antimicrobial activity of wood treated with the banana peel extract against bacterial strains.	• Banana peel extract was found to contain a high amount of ruitin (973.08 mg/100 g DE) using HPLC measurement. • Peel extracts from three banana varieties, in both powder and ash forms,

				contained phytochemicals like phenols, terpenoids, and saponins and demonstrated antifungal activity against *A. niger.*
Gęgotek et al.	2017	Primary	To assess the impact of rutin on proinflammatory and proapoptotic processes in UV-irradiated fibroblasts.	● Rutin decreased UV-induced proinflammatory response and ROS generation while increasing the activity and levels of antioxidants.
Merhan	2017	Secondary	To describe how the structure of carotenoids affects oxidative stress and their role in reducing the risk of various diseases.	● Carotenoids' antioxidant properties stem from their double carbon-carbon bonds, which allow electrons to move freely through conjugation.
Dahham et al.	2015	Primary	To assess the antioxidant capacity of banana extracts, evaluate their ability to inhibit the proliferation of colon (HCT-116) and human breast (MCF-7) cancer cell lines, as well as a normal cell line (human umbilical vein endothelial cells, HUVEC).	● The hexane extracts of banana peels showed the highest activity, with 85.32% inhibition at 100 µg/mL. ● Banana peel extract using n-hexane exhibited 48.22% toxicity against MCF-7 human breast cancer cell lines, with no cytotoxic effect on normal cell lines. ● Banana peels are a good source of antioxidant and antiangiogenic agents.
Anal et al.	2014	Secondary	To enhance the yield of phenolic extracts from banana peels and cinnamon barks using different extraction methods and to evaluate the antioxidative potentials of these extracts in fish oil.	● The importance of various components in banana peels, including minerals, vitamins, and organic acids, which contribute to the stability of phenolic acids.
Enaru et al.	2021	Secondary	To summarize the antioxidant capacity of anthocyanins and	● Several factors, such as temperature, oxygen, ascorbic acid, and light,

			the factors that can affect their stability and degradation.	can affect the stability of anthocyanins and cause them to degrade.
Vu et al.	2018	Secondary	To discuss phenolic compounds in banana peels, their current applications, and potential uses in the food and pharmaceutical industries.	● Banana peel contains a high amount of phenolic compounds, with total phenolic content varying from 4.95 to 47 mg gallic acid equivalent per gram of dry matter (mg GAE/g DM). ● Banana peels exhibit greater radical scavenging activity and reducing ability than other fruit peels. ● Processing and cooking banana peels can decrease the bioavailability of phenolic acids and diminish their antioxidant activity.
Ioannou et al.	2020	Primary	To study the effect of heat treatment and light on the antioxidant activity of flavonoids.	● Temperature and light can cause degradation in flavonoids through different pathways.
Chaaban et al.	2016	Primary	To evaluate the effects of heat processing on the antioxidant activity and stability of flavonoids.	● Glycosylated flavonoids are more heat-resistant than aglycone flavonoids.
Tang et al.	2016	Primary	To investigate the effects of the binding between flavonoid (cyanidin-3-O-glucoside) with proteins such as bovine serum albumin (BSA), haemoglobin (Hb), and myoglobin (Mb) using multi-spectral techniques and molecular modelling.	● C3G flavonoid has better stability when they form complexes with protein.
Weber & Larsen	2017	Secondary	To provide a comprehensive summary of studies	● The activity of PPO and other fruit enzymes accounts for a significant

			on the effects of juice processing on anthocyanins.	portion of the total anthocyanin losses during fruit juice production. ● Anthocyanin can be stabilized using polymerization, cleavage, and derivatization modifications.
Nagarjuna et al.	2016	Primary	To investigate the solubility and stability profile of naringin and rutin in different pH media using UV-visible spectrophotometry.	● Naringin and rutin were stable in both HCl Buffer pH 1.2 and Phosphate buffer pH 6.8.
Yousuf et al.	2015	Secondary	To provide a review of the health benefits of anthocyanins and their encapsulation for potential use in food systems.	● Flavonoids have low bioavailability. Anthocyanins are more absorbable in non-acylated forms.
Gullón et al.	2017	Secondary	To provide a comprehensive review of the extraction, identification, and purification methods of rutin, as well as its biological activities and approaches to enhance its bioavailability.	● Rutin's poor bioavailability is mainly due to its low solubility in water. Rutin's limited membrane permeability also hinders its absorption. Rutin is extensively metabolized during oral absorption, further reducing its bioavailability.
Kandemir et al.	2022	Secondary	To review the recent advances in the improvement of quercetin bioavailability.	● Quercetin has a bioavailability of less than 10% due to its water insolubility. ● Its bioavailability is highly dependent on its chemical structure.
Soukoulis & Bohn	2018	Secondary	To provide a comprehensive overview of the micro-and nano-technological encapsulation advances for	● Carotenoids are naturally occurring organic pigments composed of eight isoprene units linked to a 40-carbon-atom framework. They are

			enhancing carotenoid chemical stability and bioavailability.	extremely unsaturated, making them prone to isomerization and oxidation, which is primarily caused by light, enzymes, metals, and lipid hydroperoxides. ● The varying oxidation susceptibilities of different carotenoids, such as lutein and violaxanthin, are more labile than others. ● Dietary fibre can limit carotenoid resorption by forming poorly soluble complexes, thereby reducing their absorption in the body.
Westphal & Böhm	2015	Secondary	To provide an overview of the current knowledge on carotenoids, including their functions, health benefits, and factors influencing their bioavailability and metabolism.	● Carotenoids are classified into two types according to their structure: oxygen-free carotenes and oxygen-containing xanthophylls. ● The carotenoid structure is defined by a long chain of alternating double and single bonds that form a conjugated system. ● Carotenoids are lipophilic, and their absorption is closely linked to lipid digestion, with their antioxidant activity primarily occurring in cell membranes and lipoproteins. ● Food processing steps and endogenous metabolic reactions can result in the isomerization of carotenoids, altering their stability and bioavailability.
Cervantes-Paz et al.	2017	Secondary	To review the effects of pectin on lipid	● One of the most relevant factors limiting the

			digestion and its potential implications for carotenoid bioavailability during the pre-absorptive stages.	bioavailability of carotenoids at the pre-absorptive stages is the food matrix. ● The lipophilic nature of carotenoids requires the presence of dietary fat for absorption and transport.
Youness et al.	2021	Secondary	To provide a comprehensive review of recent advances in tannic acid (gallotannin) anticancer activities and drug delivery systems for efficacy improvement.	● Tannic Acid (TA) has been recently identified as a promising polyphenolic phytochemical with a well-defined role in each transition step of the carcinogenesis process. ● TA retains several pharmacological actions that position it as a potential antitumorigenic agent, mediated via various mechanisms, including: Radical scavenging, antioxidant effects, and anti-inflammatory effects. ● TA also inhibits the VEGF/VEGFR pathway, which is a major angiogenesis signaling pathway.
Madu et al.	2020	Secondary	To highlight the mechanism of angiogenesis in diseases, specifically its role in the progression of malignancy in breast cancer, and to highlight the ongoing research in the development of angiogenesis-targeting therapies.	● Angiogenesis, the rapid formation of new blood vessels, is essential for providing sufficient oxygen and nutrients to support the growth of breast tumors. Like all body tissues, breast cancer cells require a constant supply of nourishment and oxygen through the vascular network of capillaries.
Lin et al.	2010	Secondary	To investigate the effect of ferulic acid on angiogenesis through the modulation of	● The amounts of hypoxic-induced factor (HIF) 1 alpha mRNA and protein, the major regulators of VEGF and

			vascular endothelial growth factor (VEGF), platelet-derived growth factor (PDGF), and hypoxia-inducible factor 1 alpha (HIF-1 alpha).	PDGF, also showed up-regulation by ferulic acid.
Yang et al.	2015	Secondary	To identify ferulic acid as a novel agent with potential anti-angiogenic and anti-cancer activities and to understand the underlying molecular basis of its effects on endothelial cell proliferation, migration, and tube formation, as well as its impact on melanoma growth and angiogenesis.	● Ferulic acid targets the FGFR1-mediated PI3K-Akt signalling pathway, leading to the suppression of melanoma growth and angiogenesis.
Zaini et al.	2022	Secondary	To investigate the potential of banana peels as a bioactive ingredient and its potential application in the food industry	● The peel is rich in dietary fibre and phenolic compounds, exhibiting high antioxidant, antibacterial, and antibiotic properties. Therefore, it holds significant potential for use in the nutraceutical and pharmaceutical industries.
Gong et al.	2018	Secondary	To investigate the effects of carotenoid lutein on breast cancer cell growth and its potential to enhance the efficacy of chemotherapeutic agents through mechanisms involving reactive oxygen species (ROS).	● Lutein significantly reduces breast cancer cell growth by causing cell-cycle arrest and caspase-independent cell death. ● The carotenoid lutein selectively inhibits the growth of breast cancer cells. These intracellular signals involve increased ROS generation, activation of p53 signalling, and increased HSP60 expression. ● Lutein may be a non-toxic, selective agent

				that can induce cell cycle arrest and apoptosis in breast cancer, including triple-negative breast cancer cells.
Ahmad et al.	2019	Secondary	To provide essential information on bananas, including their varieties, distribution, pharmacological effects, and significance in the pharmaceutical industry.	● The antioxidant properties of ambon banana peel extracts can reduce oxidation markers, increase antioxidant enzyme activities, as well as reduce glutathione levels in rats.
Rebello et al.	2014	Primary	To investigate the in vitro antioxidant activity of banana peel flour (*Musa AAA*).	● The phenolic compounds in banana peel flour (Musa AAA) were notably high, approximately 29.17 mg/g GAE.
Bezerra et al.	2013	Primary	To characterize green banana flour produced by spouted bed drying and to evaluate its functional properties.	● Flours obtained through sprouted drying and lyophilization techniques have a higher phenolic acid content compared to the hot air oven or solar drying methods.
Vu et al.	2017	Primary	To investigate the effect of different drying methods on the quality of banana peels.	● The best method to retain the phenolic content is the microwave irradiation of 960 W for 6 minutes, followed by freeze-drying, a vacuum oven at 60C, a hot air oven at 120°C, dehumidified air at 60°C, and sun drying.
Ahmed et al.	2021	Primary	To demonstrate the nutritional value of banana peel powder (BPP) by emphasizing its antimicrobial and antioxidant properties.	● Banana peel powder naturally contains a total of 1783.32 mg/100 g of flavonoids and 846.58 mg/100 g of carotenoids.
Loza et al.	2017	Primary	To develop functional cookies with banana flour and sesame	● Cookies made with a 20% substitution of banana flour and 8%

			seeds with good storage stability.	sesame oil had the highest antioxidant capacity against DPPH radicals compared to the control. ● It is possible to develop good storage-stability cookies with improved functional characteristics using banana flour and sesame seeds.
Shafi et al.	2022	Primary	To evaluate the impact of incorporating banana peel flour (BPF) on the nutritional and antioxidant properties of cookies made with wheat flour.	● Cookies enriched with banana peel flour have a higher DPPH scavenging ability and total phenolic content (TPC) ● Cookies enriched with banana peel flour can have enhanced antioxidant properties without affecting their physical and organoleptic qualities.
Chakraborty et al.	2017	Primary	To determine the most optimal methods for processing banana peels into chips while preserving their nutritional values.	● Moisture loss and shrinkage of banana chips are more likely to occur with longer drying times, higher temperatures, or higher microwave wattage. ● Banana peels dried into chips using microwave drying at 540 watts for 6 minutes had a higher polyphenol content (12.6 mg GAE/g dry weight) than banana chips without the peel (6.12 mg GAE/g dry weight).

BREAST CANCER

Causative factors

Several studies have identified several genetic factors that may increase the potential of developing breast cancer, including mutations in the BRCA1 and BRCA2 genes (Wardati, 2017). Mutation from one of these genes will cause the women to have a higher potential for breast cancer development than women without the mutation. According to Momenimovahed and Salehiniya (2019), there are more inherited gene mutations that can raise the risk of breast cancer, including those in the TP53, PTEN, and STK11 genes.

Moreover, exposure to certain environmental factors, such as radiation, can increase the risk of breast cancer. Studies have shown that women who have been exposed to higher levels of air pollution or certain pesticides may have an increased risk of the disease. A higher probability of breast cancer is also associated with lifestyle variables like smoking, alcohol drinking, and sedentary lifestyles. Furthermore, women who are obese or overweight may be more susceptible to this disease (Dieterich et al., 2014).

Pathophysiology

A type of cancer that occurs when cells in the breast divide and grow without normal control is known as breast cancer. This cancer has two types: invasive and non-invasive. Invasive breast cancer occurs when the spread of a cancer cell is into other parts of the body beyond the breast, such as the invasive MDA-MB-231 cells obtained from human breast carcinoma. Meanwhile, non-invasive breast cancer is contained in the breast tissue and has not spread to other parts of the body, such as non-invasive MCF-7 cells derived from human breast adenocarcinoma, which are frequently used in research due to their accessible, stable, and broad application (Sapudom et al., 2019). The mechanism of cancer is a multistep process called carcinogenesis, which involves initiation, promotion, and progression steps.

The first stage of carcinogenesis, or initiation stage, involves exposure to a single carcinogenic agent, which causes DNA damage in the cells and their progeny, which free radicals can induce. If free radical-induced DNA damage in breast cells is not adequately repaired, it may result in mutations in vital genes that regulate cell development and division. Antioxidants can prevent free radical-induced DNA damage. Antioxidants are chemicals that can protect DNA, proteins, and lipids from oxidative damage by providing an electron to neutralize free radicals (Griñan-Lison et al., 2021). The next stage is the promotion stage, which is caused by repeated exposure to non-carcinogenic substances that temporarily alter the cellular network. Finally, the progression stage results in the formation of a malignant neoplasm, which is distinguished by structural changes in the cell nucleus, and the tumour's malignancy can worsen with repeated exposure (Wardati, 2017). In addition, carcinogenesis is driven by exogenous and endogenous factors, which may lead to the formation of highly reactive species that bind covalently to the cell's DNA, resulting in changes in DNA sequence and function through the activation of protein kinase C (PKC). This activation can lead to changes in the membrane and cell proliferation, leading to altered cell differentiation (Goff & Danford, 2021).

AMBON BANANA PEEL (*Musa paradisiaca AAA)*

Banana peel is the outer part of the banana, which is considered an agricultural by-product; hence, it is being discarded into landfills due to inadequate valorization. Although so, banana peel can be potentially utilized as a functional food due to its nutritional value and various health benefits, especially to humans (Hikal et al., 2022). A study performing the proximate, crude fibre, and pectin analysis on the ambon banana showed that its peel contained a high amount of water (69.93%), carbohydrate (25.09%), and fibre (12.02%). In contrast, the ash, fat, protein, and pectin contents were not as high as other banana cultivars (Proverawati et al., 2019). The details are illustrated in **Table 1.**

Table 2. Nutritional components of ambon banana peels

Parameters	Content (%)
Water	69.93

Ash	3.22
Fat	1.38
Protein	1.30
Crude fiber	12.02
Carbohydrate	25.09
Pectin	1.00

Source: Proverawati et al. (2019).

BIOACTIVE COMPOUND OF AMBON BANANA PEEL

Ambon banana peel is known to be an excellent source of antioxidants (Rebello et al., 2014; Mondal et al., 2021). It has been reported that bananas from *Musa paradisiaca* species contain high antioxidant properties in all stages of maturity, with raw banana peels being the most active as opposed to the mature and very mature ones (Hikal et al., 2022). One study stated that the antioxidant activity of *Musa paradisiaca* reached up to IC_{50} of 64.03 ppm (Alamsyah et al., 2016). A phytochemical analysis done by Prakash et al. (2017) found that Ambon banana peels are high in phenols, flavonoids, and carotenoids, along with other compounds such as terpenoids and saponins that possess antioxidant properties. Therefore, the peels provide a readily accessible, appropriate, and approachable foundation for the control and management of cancer (Pereira & Maraschin, 2015).

Table 3. Comparison between a bioactive compound in ambon banana peels

Bioactive Compound	Antioxidant Properties	Stability and Bioavailability
Phenolics	High antioxidant capacity	Stable in the presence of minerals, vitamins, and organic acids; sensitive to oxygen and light; extraction conditions affect purity
Flavonoids	Scavenge free radicals, reactive oxygen species (ROS), and reactive nitrogen species (RNS)	pH, light, air, temperature, and interfering compounds affect stability; glycosylated flavonoids are more stable than aglycone ones; low bioavailability
Carotenoids	Scavenge free radicals, inhibit singlet oxygen and peroxyl radicals	Lipophilic, require dietary fat for absorption; thermal and mechanical crushing improve bioavailability; dietary fibre limits resorption
Tannins	Scavenge free radicals, reduce oxidative stress	Stable in the presence of other compounds; specific extraction conditions required
Ferulic Acid	Scavenge free radicals inhibit enzymes that accelerate free radical production	Stable in the presence of other compounds; specific extraction conditions required

Rutin	Scavenge free radicals, reduce oxidative stress	Poor bioavailability due to low solubility and limited membrane permeability
Anthocyanins	Scavenge free radicals, reduce oxidative stress	Low stability; regulated through derivatization, polymerization, and cleavage
Quercetin	Scavenge free radicals, reduce oxidative stress	Poor bioavailability due to low solubility and limited membrane permeability
Lutein	Scavenge free radicals, inhibit singlet oxygen and peroxyl radicals	Lipophilic, require dietary fat for absorption; thermal and mechanical crushing improve bioavailability; dietary fibre limits resorption

Phenolics

The total phenolic content of Ambon banana peel was reported to be 19.6 mg/g expressed in Gallic Acid Equivalent (GAE), with an antioxidant capacity of 67.88% and 54.30% when evaluated using the ABTS and DPPH assays, respectively (Fidrianny & Insanu, 2014). Furthermore, Vu et al. (2018) mentioned that banana peel is rich in phenolic compounds, with a total phenolic content of approximately 4.95 - 47 mg GAE/g dry matter (DM). The phenols in Ambon banana peel, such as tannins, qoumarine, and quinone, act as antioxidants by scavenging free radicals due to the hydroxyl groups they contain, which function as reducing agents and donate hydrogen to free radicals (Prakash et al., 2017). A study by Pereira and Maraschin (2015) also reported that banana peels contain other bioactive compounds, such as anthocyanins, alkaloids, and phlobatannins, which provide various pharmacological benefits in reducing the oxidative activity inside the cells.

Furthermore, a study conducted by Corona et al. (2015) discovered the presence of 0.38% ferulic acid, which is a phytochemical with antioxidant properties, in the banana peel extract of *Musa paradisiaca L.* using ultra-performance liquid chromatography with electrospray ionization. As an antioxidant, ferulic acid (3-methoxy-4-hydroxycinnamic acid) not only serves as a scavenger of radicals but also inhibits enzymes that accelerate the production of free radicals (Zduńska et al., 2018).

Flavonoids

Flavonoids, such as anthocyanins and flavan-3-ols monomers and polymers, can be found in different parts of bananas, including the peel (Rebello et al., 2014). Furthermore, other flavonoids (flavanone glycoside and flavonol glycoside) are also found in banana peel and can undergo enzymatic or chemical auto-oxidation to produce a flavonoid semiquinone radical, which can be eliminated by reduced glutathione (GSSH). This results in the regeneration of the flavonoid and the production of a thiyl radical of glutathione that then reacts with GSSH to create a disulfide radical anion, which quickly reduces molecular oxygen to form a superoxide anion radical. Furthermore, the antioxidant activity of flavonoids is also dependent on their configuration and the number of hydroxyl groups, where the presence of B-ring hydroxyl configuration is known to exert a scavenging ability towards reactive oxygen species (ROS) and reactive nitrogen species (RNS) (Kumar et al., 2013).

A type of flavonoid known as rutin is also found abundantly in banana peels. A study done by Behiry et al. (2019) discovered that *Musa paradisiaca* peels contained 973.08 mg/100 g dry extract of rutin using a high-performance liquid chromatography (HPLC) technique, which is considered high. Rutin exerts its antioxidant properties by lowering oxidative stress and donating electrons to free radicals, transforming them into a more stable molecule (Gęgotek et al., 2017).

Carotenoids

Ambon banana peel also contains carotenoids, such as lutein, beta-carotene, alpha-carotene, violaxanthin, auroxanthin, neoxanthin, isolutein, beta-cryptoxanthin, and alpha-cryptoxanthin, which exhibit free radical scavenging properties. Banana peels can contain 6.203 ± 0.004 µg/g of carotenoids, which can provide a vitamin A conversion of 124.06 ± 0.08 IU (Sula et al., 2018). Carotenoids possess the ability to obstruct active radicals by means of electron transfer, provision of hydrogen atoms to radicals, or attachment to radicals. The level of suppression of superoxide by carotenoids is highly associated with the number of conjugated double bonds present in structural composition, which enables the elimination and prevention of singlet oxygen and peroxyl radicals from the reaction medium (Merhan, 2017). Nowadays, it is generally accepted that the complex blend of phytochemicals found in banana peel extracts work together to prevent cancer more effectively than their individual components do, as they have both additive and synergistic effects (Dahham et al., 2015).

STABILITY AND BIOAVAILABILITY OF BIOACTIVE COMPOUNDS IN AMBON BANANA PEEL

Phenolics

Phenolic acids as natural antioxidants in banana peel have been found to be effective in inhibiting oxidation caused by reactive oxygen species (ROS), thus protecting the banana from spoilage (Vu et al., 2018). The stability of phenolic acids in banana peels is attributed to the presence of several other components, such as minerals, vitamins, and organic acids. These components provide a protective environment for the phenolic acids to maintain stability and prevent them from breaking down (Anal et al., 2014).

Additionally, oxygen and light are factors that influence the stability of phenolic acids, which cause degradation and become less effective at providing antioxidant protection (Enaru et al., 2021). Moreover, phenolic acid content varies greatly depending on the ripeness, variety, and growing conditions of the banana. Therefore, different extraction conditions are needed to obtain pure phenolic compounds from the banana peel since the phenolic compounds in the banana peel are diverse. The ripening process was found to decrease the phenolic content in banana peel. Processing and cooking of the banana peel can degrade the bioavailability of phenolic acid and reduce its antioxidant activity (Vu et al., 2018).

Flavonoids

The stability of flavonoids is dependent on various factors, namely the pH, light, air (oxygen levels), temperature, and the presence of interfering compounds, thereby requiring proper food processing techniques to retain the content in banana peels (Ioannou et al., 2020). Apart from that, the structural arrangement also plays a crucial role in determining their stability. Although flavonoids are principally heat sensitive, Chaaban et al. (2016) found that glycosylated flavonoids (e.g., rutin, naringin, and luteolin 7-O glycoside) provided higher thermal stability compared to the aglycone flavonoids (e.g., mesquitol, eriodictyol, and luteolin), which can be degraded at temperatures of 30^{o}C. Generally, flavonoids can be degraded at a temperature of 50-150^{o}C, although flavonoids with higher activation energy have a higher stability towards heat. An *in vitro* study has also found that flavonoids have better stability when they form complexes with proteins (Tang et al., 2016). Anthocyanins, a type of flavonoid, have an extremely low stability. However, its stability can be regulated through derivatization, polymerization, and cleavage (Weber & Larsen, 2017). Quercetin, a yellow-coloured flavonoid, is reported to have stability at pH 1-6, similar to naringin and rutin, which showed stability in HCl buffer and phosphate buffer at pH 1.2 and 6.8, respectively, when evaluated using UV visible spectrophotometer (Nagarjuna et al., 2016).

The bioavailability of flavonoids is generally known to be low and may vary greatly between classes. Anthocyanins are more biologically absorbable in their non-acylated forms compared to acylated ones

(Yousuf et al., 2015). Rutin has also been reported to have poor bioavailability due to its low solubility and limited membrane permeability (Gullón et al., 2017). Similarly, another flavonoid compound, quercetin, also has a bioavailability of <10% as it is insoluble in water and is highly dependent on its chemical structures (Kandemir et al., 2022).

Carotenoids

Carotenoids are naturally occurring organic pigments composed of eight isoprene units linked to a 40-carbon-atom framework (Soukoulis & Bohn, 2018). Carotenoids are classified into two types: oxygen-containing xanthophylls (lutein, cryptoxanthin, and astaxanthin) and hydrocarbon carotenoids (alpha- and beta-carotene, lycopene, and phytoene). The carotenoid structure is defined by a long chain of alternating double and single bonds that forms a conjugated system that is able to delocalize an electron system, giving carotenoids their distinct physicochemical features (Westphal & Böhm, 2015). Carotenoids are extremely unsaturated, resulting in an easily isomerized and oxidized compound. The primary cause of oxidative degradation is enhanced by light, then allowed with enzymes, metals, and lipid hydroperoxides. Carotenoids appear to have varying oxidation susceptibilities, with lutein and violaxanthin being more labile than others (Soukoulis & Bohn, 2018). In addition, carotenoids are lipophilic, meaning they are insoluble in water but soluble in organic solvents (Westphal & Böhm, 2015).

The bioavailability of carotenoids is controlled by a variety of circumstances and can be improved by particular methods. Due to their hydrocarbon composition, carotenoids are non-polar and require dietary fat to be absorbed into the intestinal lumen by integrating into lipid droplets and enterocytes as micelles (Cervantes-Paz et al., 2017). Furthermore, food processing processes often improve carotenoid bioavailability. In order to improve its bioavailability, thermal and mechanical crushing are able to degrade cell walls, which helps the release of carotenoids from intracellular organelles, breaking down carotenoid-protein complexes and lowering particle size (Westphal & Böhm, 2015). Besides the improvement, dietary fibre, on the other hand, can limit carotenoid resorption by forming poorly soluble complexes with carotenoids that the body is unable to absorb and also binding to bile acids that can cause lipids and fat-soluble substances like carotenoids to be excreted (Soukoulis & Bohn, 2018).

MECHANISMS AGAINST BREAST CANCER

Recent research has highlighted the antioxidant properties of ambon Banana peels, which have been demonstrated to reduce the potential for tumour cell development by scavenging free radicals, which result in the inhibition of breast cancer cells (MCF-7) proliferation (Mondal et al., 2021). Triterpenoids, a subclass of the terpenoid family, have emerged as promising chemopreventive agents, as they have been shown to trigger apoptosis in breast cancer cells while leaving normal cells unharmed. Multiple mechanisms are involved in the selective targeting and elimination of breast cancer cells by triterpenoids, effectively preventing healthy cell disruption (Aly et al., 2024).

Tannins, another important polyphenol in ambon banana peel, have been known to exert anti-cancer activity by inducing apoptosis and inhibiting the VEGF/VEGFR pathway, which is the main angiogenesis pathway in breast cancer (Youness et al., 2021). Angiogenesis itself is the formation of blood vessels that increase rapidly to nourish breast tumour growth (Madu et al., 2020).

Ferulic acid found in banana peels has been acknowledged for its potential to regulate the expression of vascular endothelial growth factor (VEGF), which is normally highly up-regulated in breast cancer (Lin et al., 2010). Yang et al. (2015) mentioned that ferulic acid exerts an inhibitory effect on the fibroblast growth factor receptor 1 (FGFR1), suppressing tumour formation. It also initiates the production of endothelial nitric oxide synthase (eNOS), thereby inhibiting the cancer-inducing events in breast cancer, such as inflammation, apoptosis, and metastasis (Zaini et al., 2022).

The flavonoid content of banana peel has also been found to increase the expression of the p53 protein, which plays an important role as a tumour suppressor in T-47D cancer cell lines. Flavonoids have been shown to have strong anticancer activity by inducing apoptosis of the T-47D cell by inhibiting the expression of topoisomerase I and II, leading to the release of pro-apoptotic proteins such as Bax and Bak (Wardati, 2017). In addition, studies have shown that among various types of carotenoids, lutein has a strong chemoprotective effect on breast cancer by initiating cell cycle arrest and inducing caspase-independent cell death. It also accelerates the activation of the p53 signalling pathway, promotes cell type-specific ROS generation, and enhances the cytotoxic effects, inhibiting metastatic breast cancer (Gong et al., 2018). The mechanisms of Ambon banana peel against breast cancer are as illustrated in **Figure 2.**

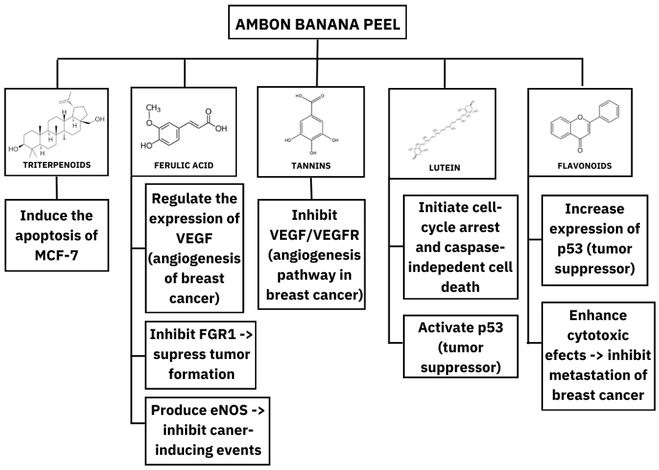

Figure 2. Mechanism of Ambon banana peel against breast cancer

CLINICAL STUDY AND EFFECTIVENESS OF AMBON BANANA PEELS ON BREAST CANCER

A study was conducted by Ahmad et al. in 2019 to investigate the antioxidant properties of Ambon banana peel extracts in rats. One category of rats received a standard diet, while another group was fed a diet with a high concentration of fatty acids. The researchers gauged oxidation markers like malondialdehyde (MDA) and found that rats treated with an extract from banana peel experienced a notable decrease in peroxidation product levels (MDA), peroxides, and conjugated dienes. Moreover, antioxidant enzymes' activities, such as catalase and superoxide dismutase, increased substantially in the treated rats. Additionally, the levels of reduced glutathione (GSH), a vital antioxidant, were enhanced. Another experiment was conducted by using ethanol and ethyl acetate to extract powdered *Musa paradisiaca* in an ultrasonic bath. The findings demonstrated that the ethanol extract had a more significant antioxidant activity (IC50-50% inhibitory concentration) than the ethyl acetate extract, with values of 3374.13 ± 123.46 and 40318.19 ± 1014.90 ppm, respectively. Dahham et al. (2015) discovered that the banana peel extracted using n-hexane displayed a toxicity of up to 48.22% against MCF-7 human breast cancer cell lines, with no cytotoxic effects observed against the normal cell lines. Despite the success of these experiments, further research is still needed as the current clinical studies in humans are still lacking.

APPLICATION OF BANANA PEELS IN FOOD PRODUCTS AS ANTIOXIDANT SOURCES

Banana peel flour

Due to the perishable nature of banana peel, its transformation into banana peel flour is crucial to improving its storability potential, hence prolonging its shelf life. Banana peel flour is a value-added product that also serves as a sustainably nutritious edible material that can be used for food fortification or enrichment purposes. A study discovered that the phenolic compounds in banana peel flour (*Musa AAA)* were considerably high, amounting to approximately 29.17 mg/g GAE, as it contained numerous flavonoid compounds, mainly the highly polymerized prodelphinidin (3,952 mg/kg) (Rebello et al., 2014). The processing methods of banana peel flour also greatly affect the antioxidant activity and the total phenol content. Flours acquired by sprouted drying and lyophilization techniques have been found to have higher phenolic acid content compared to those using hot air ovens or solar drying (Bezerra et al., 2013). Furthermore, the use of microwave ovens was correlated with higher retention of bioactive compounds, TPC, and antioxidant activity, whereas samples treated with dehumidified dried were reported to have the lowest phenolic content (Vu et al., 2017). Another study found that banana peel powder naturally contains a total of 1783.32 and 846.58 mg/100 g of total flavonoids and carotenoids, respectively, hence holding various importance in terms of health and well-being (Ahmed et al., 2021).

Cookies

Banana peel flour can be used to produce other derivative products, such as snacks, bread, cookies, and biscuits. A study has found that cookies with 20% substitution of banana flour (*Musa paradisiaca)* and 8% sesame oil obtained the highest antioxidant capacity towards DPPH radicals (IC_{50} = 17.52±0.25 mg/mL) compared to the control (IC_{50} = 24.115 ± 0.55) (Loza et al., 2017). This result was further supported by the findings from Shafi et al. (2022), claiming that cookies enriched with banana peel flour obtained significantly higher DPPH scavenging ability and TPC, ranging from 62.02 ± 0.32 to 70.29 ± 0.84% and 0.561 ± 0.020 to 0.921 ± 0.007 mg GAE/g, respectively.

Banana peel chips

Banana peel can be further utilized in chips with potential sources of antioxidants (Zaini et al., 2022). In a study, Chakraborty et al. (2017) established that banana peel that has been dried into chips provided higher polyphenol content (12.6 mg GAE/g dry wt basis) compared to the banana chips without the peel (6.12 mg GAE/g dry wt basis) when treated with microwave drying with 540 Watt for 6 minutes. The same study also revealed that this drying method provided a higher polyphenol retention ability compared to the hot air oven drying at 70 ^oC.

CONCLUSION

In conclusion, the ambon banana peel (*Musa paradisiaca AAA*) is a rich source of phytochemicals with antioxidant properties, such as triterpenoids, ferulic acid, flavonoids, and tannins. These bioactive compounds have been shown to have antioxidant and free radical scavenging properties. Moreover, ambon banana peel has also demonstrated antioxidant properties in *in vivo* studies and holds potential for further exploration to prevent cancerous diseases. Additionally, several studies have shown the potential of ambon banana peel extract to have cytotoxic effects on MCF-7 human breast cancer cell lines. However, clinical studies regarding this topic are still limited and need further research. Moreover, Ambon banana peel can be found in the form of flour or cookies as a natural source of antioxidants with a longer shelf life.

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