SYSTEMATIC STUDY OF THE ANTIOXIDANT POTENTIAL AND INCREASING BIOACTIVITY OF RICE FOR SKIN HEALTH

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Abstract
Agar beras dan dedak baik dari beras pigmented maupun unpigmented dapat memberikan dampak positif pada kulit maka harus dibuat lebih bioaktif. Penelitian ini dilakukan sebagai tinjauan literatur sistematis dengan menggunakan teknik PRISMA (Preferred Reporting Items for Systematic Review and Meta-analyses), dan seluruhnya mengikuti langkah atau prosedur yang benar. Penelitian SLR ini menggunakan pendekatan deskriptif dan termasuk dalam penelitian kualitatif di bidang perpustakaan. Persoalan utama yang telah diidentifikasi dan dijadikan pedoman proses penelitian diamati dalam berbagai literatur. Selanjutnya, kriteria inklusi dan eksklusi digunakan untuk melakukan seleksi. Beras dan dedak berpotensi menghambat enzim tirosinase karena mengandung asam fenolik, γ-oryzanol, dan tricin. Senyawa antosianin pada beras dan dedak berpigmen memiliki potensi sifat anti penuaan dan anti inflamasi melalui jalur sinyal MAPK. Senyawa lain berupa momilactone A dan B yang terkandung dalam bekatul berpotensi menjadi anti penuaan dan pencerah kulit. Peningkatan bioaktivitas dapat dilakukan dengan metode fermentasi menggunakan berbagai mikroorganisme, metode protein dedak dengan menggunakan enzim papain atau campuran trypsin dan chymotrypsin untuk memperoleh peptida dalam dedak yang mampu menghambat tirosinase, serta metode padi transgenik yang diperkaya resveratrol untuk menghasilkan efek sinergis antara beras dan resveratrol. Berdasarkan hasil penelusuran artikel, penelitian terkait senyawa antioksidan yang diformulasikan mampu memberikan potensi khasiat pada kulit manusia setelah dilakukan pengujian in vitro dan in viv
Kata kunci: Tinjauan Sastra Sistematik, Beras, Dedak Padi, Antioksidan, Kesehatan Kulit

Abstract
In order for rice and bran from both pigmented and unpigmented rice to have a positive impact on the skin, it must be made more bioactive. This study was conducted as a systematic literature review utilizing the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analyses) technique, and it adhered to the right steps or procedures throughout. This SLR research uses descriptive approaches and is categorized as qualitative research in libraries. The main issue that has been identified and served as a guide for the research process is observed in numerous pieces of literature. Next, inclusion and exclusion criteria are used to make the selection. Rice and bran have the potential to inhibit the tyrosinase enzyme because they contain phenolic acids, γ-oryzanol, and tricin. Anthocyanin compounds in pigmented rice and bran have potential anti-aging and anti-inflammatory properties through the MAPK signaling pathway. Other compounds in the form of momilactone A and B contained in rice bran have the potential to be anti-aging and skin-lightening. Increasing bioactivity can be done by fermentation methods using various microorganisms, bran protein methods using the papain enzyme or a mixture of trypsin and chymotrypsin to obtain peptides in the bran that are capable of inhibiting tyrosinase, as well as transgenic rice methods enriched with resveratrol to produce a synergistic effect between rice and resveratrol. According to the results of the article search, studies related to formulated antioxidant compounds were able to provide potential efficacy on human skin after in vitro and in vivo testing.
Keywords: Systematic Literature Review, Rice, Rice Bran, Antioxidants, Skin Health

INTRODUCTION

One of the numerous Asian nations where rice (Oryza sativa L.) is a staple diet is Indonesia. White rice accounts for about 85% of all rice consumption, with colored rice making up the remainder. Red and purple-black rice are examples of colored rice available on the market. Black rice, which comes in colored variations, has a higher phenolic content than other types of rice. Black rice's total phenolic content in ethyl acetate extract is 2.29 g GAE/100 g, compared to 1.73 g GAE/100 g for white rice (Fidrianny et al., 2016). Phenolic compounds and/or polyphenols themselves are the main antioxidant compounds found in rice (Darajat et al., 2022). Apart from rice, most of the micronutrients, fatty acids, fiber, and compounds with antioxidant activity such as phenolics, tocol, and γ-oryzanol are also found in the rice pericarp, especially in pigmented rice (Muliani et al., 2021). Many studies have used the pericarp part of rice (bran) to utilize its antioxidant activity, apart from the fact that bran is generally not used because what is used in food is rice that has been ground and polished (Amanda et al., 2022). Phenolic acid, anthocyanins, and proanthocyanidins are a few polyphenolic substances with antioxidant activity that are present in rice and bran, along with additional substances including flavonoids, tocopherols, tocotrienols, -oryzanol, vitamin E, and phytic acid. However, a number of phenolic substances bind to cellulose, hemicellulose, and lignin to form a bond with the cell walls of rice or bran. Therefore, a technique is required to hydrolyze the covalent connections between phenolic chemicals and the cell wall matrix of rice and bran in order to enhance their chemical composition and bioactivity and achieve the greatest possible benefit (Alfalah et al., 2022).

Over the last 10 years, the effects of polyphenolic compounds in rice or bran on skin health have been discovered, including photoprotection against UV-B and inhibitors of the tyrosinase enzyme, so that melanin production is reduced and the skin appears whiter (Hasni et al., 2019). Rice and bran, both pigmented and unpigmented, are also able to act as antiaging agents due to their inhibitory activity on matrix metalloproteinase (MMP) enzymes and elastase enzymes, which can degrade collagen and elastin (Rafli et al., 2022). Other benefits obtained from rice and bran antioxidants include increased skin hydration, anti-inflammation, and even atopic dermatitis. Several of these studies, both in vitro and in vivo, have also tested the dosage form. Rice is a food source of energy that has a high carbohydrate content but low protein. There are several varieties of rice found in Indonesia, including white rice (Oryza sativa L.), red rice (Oryza nirvara), and black rice (Oryza sativa L. indica) (Putra et al., 2022). The color of rice is different due to differences in the anthocyanin pigment content in the epidermis layer (aleurone). Rice is rice that comes from grass plants (Gramineae). Rice consists of three ecogeographic groups, namely Indica, Japonica, and Javanica (Hasni et al., 2021).

The morphology of rice plants consists of roots, stems, leaves, panicles, flowers, and fruit. Rice roots are classified as fibrous roots; the roots that grow from the seed sprouts are the main roots, while those that grow near the node are called seminal roots (Irwanto et al., 2023). The roots of rice plants function to support the stem, absorb nutrients and water, and provide ventilation. Wild rice plants can reach a height of around 200 cm, but intensively cultivated rice varieties are much lower, namely around 100 cm. Rice stems are generally dark green, and when they enter the generative phase, the stem color changes to yellow (Nova & Hasni, 2022). Based on research, black rice plants have a height around of 136 cm, with flag leaf lengths around 29 cm. In regions with hot weather and lots of vaporized water, rice plants can thrive. The ideal amount of rainfall each year is about 1800 mm, and the best amount of rainfall for rice plants is an average of 200 mm per month or more with a distribution across 4 months (Anggraini & Hasni, 2022). The ideal temperature for rice plant growth is 23° C, and the ideal height for rice plants is 0 to 1500 m above sea level (asl). In addition to flavonoids, tocopherols, tocotrienols, -oryzanol, vitamin E, and the acid phytate, rice (Oryza sativa L.) includes many polyphenolic compounds having antioxidant action. These include phenolic acid, anthocyanin, and proanthocyanidin. In contrast to white rice, colored variants, like black rice, have more phenolic chemicals (Negara et al., 2022). Only black rice was quantified, and the quantities of vanillic acid and free-soluble protocatechuic acid were highest there. Conjugated protocatechuic and dihydroxybenzoic acids, which are both present in red and black rice, are absent from non-pigmented rice. In brown rice, ferulic, p-coumaric, and dihydroxybenzoic, as well as protocatechuic acid and vanillic acid in black rice, are the principal bound phenolic acids (Desmawati et al., 2023).

The pericarp protects the grain and gives color to the rice, producing light brown, red, and black grains. 6.5 percent of the weight of the rice is made up of black rice bran. The outer layer (sub-aleurone) of black rice endosperm contains protein, whereas the inner portion is made up of around 75% carbohydrates, the majority of which are starches. In addition to starch, black rice also has trace levels of other polysaccharides, primarily simple sugars (glucose, fructose, and saccharose) and dietary fiber (resistant starch, cellulose, hemicellulose, and pectin) (Febrianto et al., 2023). Due to the presence of numerous nutritional and bioactive components, such as essential amino acids, vitamins (B complex, A, and E), a number of minerals (K, Fe, Zn, Cu, Mg, Mn, and P), anthocyanins, phenolic compounds, -oryzanol, tocopherol, tocotrienol, and phytic acid in the bran layer and embryo, rice has positive nutritional and functional values. Free radical compounds in normal amounts are beneficial for health in preventing inflammation and controlling the tone of smooth muscles, blood vessels, and other body organs. Excessive amounts of free radicals will cause oxidative stress starting at the cellular, tissue, and organ levels, which can accelerate the aging process and the emergence of disease (Anggraini & Hasni, 2021). Antioxidants are substances that can inhibit or slow down the occurrence of oxidative damage. Many studies relate to the content of antioxidant compounds in rice, which have the potential to provide pharmacological effects because oxidative stress is associated with several chronic diseases (Anggraini et al., 2022).

Two types of antioxidants are based on how they are made: those that are made inside the body (endogenous), like lipoid acid, glutathione, L-arginine, and superoxide dismutase (SOD); and those that come from outside the body (exogenous), like acid, omega-3 and omega-6 fats, vitamin E/C from fruits and vegetables or other foods, and so on (Hasni et al., 2016). You can divide antioxidants into two groups based on their type: synthetic antioxidants (like butylated hydroxyl anisole (BHA) and tertiary butyl hydroquinone) and natural antioxidants (like iron, copper, and zinc), vitamins (like vitamin C, vitamin E, and vitamin B), and phytochemicals. Skin is the body's largest organ and is composed of three main layers, from outside to inside, namely the epidermis (non-viable epidermis and viable epidermis), dermis, and endodermis (Amelia et al., 2021). These three layers are different in terms of anatomy, morphology, constituent compounds, properties, and functions. Known as keratinocytes, the flat, stratified epithelium of the epidermis is made up of several layers of cells. Through the mitosis of cells in the basal layer that eventually migrate to the epithelium's surface, these cells are continuously replenished. During this time, the cells differentiate, enlarge, and accumulate keratin filaments in their cytoplasm. As they approach the surface, the cells die and are continuously shed (sloughed off). The time needed to reach the surface is 25 days (Irakli et al., 2018).

The dermis layer, which can also be called the corium, is a layer of skin located between the epidermis and subcutaneous fat tissue. The layer thickness is around 2.5 mm, depending on the dermis of the body. In the dermis, mucopolysaccharide is present. fibroblasts and mast cells are found in the dermis (Nurhidayah & Umbara, 2019). Mast cells also contain substances that react slowly during anaphylaxis, such as prostaglandin E and histamine, as well as immunoglobulin E receptor sites. The elastic fibers, collagen, and reticulum fibers that serve as the skin's structural support system are produced by fibroblasts. Collagen, reticulum, and elastin are only a few of the protein fibers found in this dermis, which are kept in amorphous mucopolysaccharide basal glands. In order to protect the body from wounds, increase the flexibility of the epidermis, operate as a barrier against infection, and serve as a water storage organ (Utama, 2015). Blood capillaries, nerve endings, lymphatic vessels, sweat glands, hair follicles, and sebaceous glands are all found in the dermis. Depending on age, race, and body area, the endodermis, also known as the hypodermis layer, is the skin's lowest layer and is 1.6 cm thick. It connects the dermis to other tissues beneath it, such as muscles, and is a continuation of the dermis. It is made up of loose connective tissue including fat cells. The hypodermis has some elastic fibers and is rich in connective tissue. There are smooth muscles in several areas of the body. Fatty tissue affects the body's ability to regulate its temperature and functions as a cushion against pressure and damage from the outside world. This layer shields the internal organs of the body from mechanical impacts (Yuslianti, 2018).

METHOD

This study took the form of a Preferred Reporting Items for Systematic Reviews and Meta-analyses method-based systematic literature review, which was conducted in accordance with the right research phases or procedures. This SLR research is in the form of qualitative research, which is included in library research with descriptive methods. Observations are made from various pieces of literature related to the main problem that has been determined and used as a guide in the research process. A systematic research literature review design was carried out to determine the three research questions, namely antioxidant compounds in rice and bran, whether white, red, or black, which have the potential for skin health, increasing the bioactivity of rice and rice bran, and developing them in topical dosage forms to maximize this potential. Data collection is limited to English-language articles conducted on the research sites Pubmed, ScienceDirect, and MDPI. The literature selection strategy carried out by searching based on keywords is to skim through the titles that are appropriate to the research topic and then select them based on abstract screening and full text review to determine whether they suit the research question. Next, selection is carried out using inclusion and exclusion criteria.

RESULTS AND DISCUSSION

Based on the research results, it shows that from some articles found, polyphenolic compounds are the main antioxidant compounds found in rice and rice bran. Flavonoid chemicals and phenolic acids make up polyphenols. Ferulic, p-coumaric, vanillic, sinapic, caffeic, p-hydroxybenzoic, and protocatechuic acids are phenolic acids that can be found in rice and bran, both pigmented and non-pigmented varieties. The majority of phenolic acid compounds are ferulic acid compounds. According to earlier studies, ferulic acid, which accounts for 60% of the total phenolic acid present in endosperm, bran, and grains, is followed by p-coumaric acid, sinapic acid, gallic acid, protocatechuic acid, 2.5% p-hydroxybenzoic acid, and vanillic acid. Both water extracts with a concentration of 100 mg/ml and NaOH hydrolyzed extracts with a concentration of 0.4 mg/ml of phenolic acid components from rice and white rice bran have an inhibiting impact on the tyrosinase enzyme. A number of phenolic compounds are bound to the cell walls of rice or bran through binding with cellulose, hemicellulose, and lignin, where NaOH can release ester bonds from phenolic compounds. As a result, the inhibitory power of the tyrosinase enzyme in water extracts is lower than in extracts hydrolyzed with NaOH. For pigmented rice, phenolic acid compounds are also thought to be compounds that have the potential for tyrosinase activity, even though anthocyanins are the main compounds.

After reading several articles, it is clear that phenolic acid compounds found in rice and bran, especially white rice bran and rice, may also help slow down the aging process by blocking the enzymes elastase and matrix metalloproteinase (MMP). It is thought that blocking these two enzymes might slow down the aging process because UV light can break down skin elastin through the elastase enzyme, causing skin elasticity to drop and MMP levels to rise (a skin-aging substance) because of how the AP-1 transcription factor is controlled. Furthermore, when phenolic acids such as ferulic acid are combined with γ- oryzanol and made in the form of niosomes, their MMP inhibitory activity increases further. Apart from white rice, the phenolic acid compounds provided by pigmented rice also have anti-aging potential, although this still needs to be tested again because anthocyanin, which is the main compound, also has anti-aging activity. Several studies also say that this compound can hydrate the skin. The mechanism is still unknown, but ferulic acid in gel preparations can increase its penetration throughout the SC due to the occlusion effect of the oil and fat composition, which can increase skin hydration. The occlusion effect blocks diffuse water loss from the skin surface due to the presence of layers of oil and fat, thereby increasing hydration of the stratum corneum and increasing water uptake into intercellular lipids.

Anthocyanins and proanthocyanidins belong to the group of polyphenolic compounds. The primary antioxidant elements in colored rice, including black rice and brown rice, are anthocyanins and proanthocyanidins. According to a number of studies, the amount of anthocyanin in rice affects how dark the color is, which is related to how antioxidant-active it is. The anthocyanins present in black rice are cyanidin-3-O-D-glycoside, taxifolin-7-O-glucoside, peonidin-3-O-glucoside, and quercetin-3-beta-D-glucoside, according to investigations in the literature. They are proanthocyanidin and paeoniflorin in red rice. Because they can inhibit matrix metalloproteinases at a concentration of 100 µg/mL of ethanol extract, red rice and black rice have the potential to be used as anti-aging treatments. This is due to the fact that the anthocyanin content in red rice and black rice can inhibit NF-κB and have an effect on AP-1, which in turn controls the transcription of UVB-induced skin aging genes like MMP-1 and MMP-9 as well as inflammatory cytokines. It is suggested that administration of red and black rice extract may be able to lessen it by blocking the MAPK signaling pathway (Mitogen-Activated Protein Kinases Signaling Pathway). MAPK signaling is crucial for controlling skin aging and cell growth. Black and brown rice are also thought to be able to increase the formation of type 1 procollagen. Thus, it is thought that the anti-aging properties of anthocyanins and proanthocyanidins found in black rice and red rice have considerable potential. Apart from anti-aging, anthocyanins and proanthocyanidins also have the potential to act as anti-inflammatory agents through the NF-κB activation mechanism, which occurs due to increased ROS due to exposure to UV or other free radicals.

The γ-oryzanol compound is one of the compounds found in rice and bran, both pigmented and unpigmented. This chemical might be anti-melanogenic because it blocks the tyrosinase enzyme. It is also thought to be able to lower the expression of MITF (microphthalmia-associated transcription factor), an enzyme that controls the production of melanin. Based on research, melanin in B16F1 cells was reduced by 28% at γ-oryzanol concentrations of 3 and 30 µM for three days. Furthermore, when it is made in niosome form in gel and cream preparations, differences in the amount of melanin also occur, where the amount of melanin is lower compared to without treatment. Y-oryzanol is also able to act as photoprotection against UV exposure with an SPF value of 4.5-5.1 (medium potency) in addition to preventing melanin formation. This means that γ-oryzanol can be used as an active substance for skin-lightening (whitening) cosmetics. Tricin is a flavonoid compound that is mostly found in rice bran. The antioxidant activity of tricin itself reaches IC50 = 0.3 mg/mL, so it is considered to have quite potential in its use as an anti-melanogenic agent. At a concentration of 2 mg/mL, the isolated yield of tricin from bran was only 16% effective at inhibiting tyrosinase. Momilactone A and B are secondary metabolites or phytoalexins that are crucial for plant defense. These two chemicals were initially identified from the husks of rice seeds and are members of the diterpene family. Momilactone A and B have antioxidant action, therefore this study evaluated for elastase and tyrosinase activity inhibition and found that MA and MB would be excellent anti-aging and skin-whitening options. In vivo models and pre-clinical studies should be used to assess the application of these substances with a focus on skin penetration, skin irritability, and other side effects.

Based on article searches, several studies mention three methods for increasing the bioactivity of rice and bran, both pigmented and non-pigmented. This is so because phenolic substances and phenolic acids can be found in three different forms in rice and bran: free soluble, free conjugated, and bound and insoluble forms. In rice, several hydroxybenzoic and hydroxycinnamic acid derivatives can be identified that result in complex structures like lignin and hydrolysable tannins. Cell walls include ferulic, p-coumaric, and caffeic acid, which are hydroxycinnamic acid derivatives. Ester bonds hold these substances to the cellulose, lignin, and protein that make up cell walls. Enzymatic hydrolysis or the addition of alkaline can release these molecules, enhancing the biofunctionality of natural substances. Based on research results, rice fermentation using A. niger and R. oligosporus, apart from being able to produce active components that have significant antioxidant activity, the inhibitory activity of tyrosinase and elastase is also quite high (A. niger tyrosinase 34% and R. oligosporus 46%; Elastase A. niger 50% and R. oligosporus 52%). Based on the findings, a distinct profile was produced, with M. purpureus extract having a stronger elastase inhibitory action (23%), followed by A. niger (13%), in single-culture fermentation. Higher inhibitory power was offered by the mixed culture fermentation extract of M. purpureus and A. niger. This finding also raises the possibility that a number of active metabolites generated during the fermentation process may contribute to the inhibitory activity of elastase. This means that the mix of fungi that makes the enzyme consortium has released a number of different chemicals that help stop elastase from working.

Most of the bioactive parts in black rice bran extract that stopped tyrosinase from working were phenolic acids, according to the research results. The amount of phenolic acid that could be extracted, particularly ferulic acid and protocatechuic acid, increased significantly during fermentation using A. lumori and A. oryzae, despite the fact that the total phenolic content actually dropped following the pre-fermentation heating procedure. A. lumori has the ability to create enzymes that affect the state of phenolic compounds and are involved in metabolic and hydrolysis activities. Additionally, A. lumori's fermentation of black soybeans resulted in a rise in the amount of total phenolics and extractable anthocyanins. This was made possible because β-glucosidase stimulated the breakdown of covalent links between phenolic components and the cell wall matrix. On the other hand, heating black rice bran during pre-fermentation considerably lowers anthocyanin levels because heating can allow anthocyanins to become more easily degraded into chalcone. So, after fermentation, the amount of anthocyanin does not change significantly.

Propylene glycol was chosen as a co-solvent in the ensuing emulsion because it provided a clear solution free from precipitates when the rice extract was dissolved in it at 10 and 9% (w/w) before being formulated into a dosage form. Even though the total phenolic content of the rice extract solution in propylene glycol decreased, the physicochemical characteristics of the extract solution and accelerated stability tests revealed that it was stable with no color change. According to the formulation results, the cream may be effective on the skin. The physicochemical parameters of the emulsion change depending on the amount of rice extract present. A larger extract content results in a thicker formulation and a lower pH. The formulation remained homogeneous during expedited testing, with just a minor change in viscosity, however the acidity level rose. This was probably due to changes in the stability of the extract, which reduced the pH value according to the results of the accelerated stability of the extract. The magnitude of change is also within the acceptable range for cosmetic formulations.

CONCLUSION

Rice and bran have the potential to inhibit the tyrosinase enzyme because they contain phenolic acids, γ-oryzanol, and tricin. Anthocyanin compounds in pigmented rice and bran have potential anti-aging and anti-inflammatory properties through the MAPK signaling pathway. Other compounds in the form of momilactone A and B contained in rice bran have the potential to be anti-aging and skin-lightening. Increasing bioactivity can be done by fermentation methods using various microorganisms, bran protein methods using the papain enzyme or a mixture of trypsin and chymotrypsin to obtain peptides in the bran that are capable of inhibiting tyrosinase, as well as transgenic rice methods enriched with resveratrol to produce a synergistic effect between rice and resveratrol. According to the results of the article search, studies related to formulated antioxidant compounds were able to provide potential efficacy on human skin after in vitro and in vivo testing. The skin penetration, skin irritability, and other adverse effects of antioxidant chemicals in rice or bran formulations need to be further investigated using a variety of in vivo models and pre-clinical testing.

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