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Extraction methods of melanoidins and its potential as a natural pigment

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Abstract

In last years,consumers pay more attention to natural and body-friendly pigments. There is a great tendency to promote and popularize natural dyes instead of synthetics. But instability of these natural pigments has many negative impacts on application. However,melanoidins,high molecular weight brown nitrogenous polymers formed at the end of the Maillard reaction,are increasingly studied by scholars ascribe to its enormous biological activity. They are normally formed during heat processing of foods. This brown-colored compounds may be a natural pigment due to its desirable dark brown and biological activity. what's more,its ability is superior to other natural pigments. On the other hand,this compounds' isolation and purification are the key step for further use and biological maintenance in various kinds of industries. However,the selection of methods is mainly dependent on their structure. It is necessary to seek out some effective modification or advanced technologies to update and even take place of the traditional methods, among which a large quantity of ways about extraction is time-consuming. Hence,this review summarizes extraction methods of melanoidins,exploring the recent literature regarding the feasibility of emerging extraction methods and as a new potential natural pigment.

Keywords: melanoidins; extraction methods; natural pigment; biological activity.

Practical Application: This review summarizes the extraction methods, biological activities, potential applications and some emerging extraction methods of melanoidins which may provide references for the follow-up research.

1 Introduction

Whether the color of food is bright may have gradually become a prerequiste for people to choose. Nevertheless, a large part of these colorants are artificial, esteem that most of them are detrimental to different organs to some extent (Neri-Numa et al., 2017). Compared to artificial colorants, natural pigments may draw more attention to the people on account of the increasing consciousness concerning body-friendly and eco-friendly. Thus, considering both healthy and attractive, industries should pay more attention to occupying in searching for novel dyes for color addtives (Ngamwonglumlert et al., 2017).

In the last few years,as regards to natural pigments, anthocyanins (purple, blue and red), betalains (red-purple), carotenoids (orange and yellow) and chlorophylls (green) are prevalently used to color additives rather than synthetic ones in food industries. These four color pigments can be obtained from plants, microorganisms and insects. In addition, these natural compounds have not only coloring properties, but also some powerful biological activities such as antioxidant, anti-hypertensive, anticancer (Miranda et al., 2021). Because of these properties,a burning trend of application in cosmetic and pharmaceutical segments has gradually prevailed. What's more, it may brings considerable revenue for industries.

Melanoidins, generating at the final stage of Maillard reaction which occurs at during the process of heat of foodstuff containing reducing sugars and amino acids, are chiefly responsible for the characteristic brown color of foods such as coffee, bread, malt (Mesías & Delgado-Andrade, 2017). As these compounds can endow foods with satisfying brown color that urges consumers to mind a high-level product owning irresistible texture and flavourinterest for melanoidins is growing in some industries. Meanwhile, these brown-colored compounds, have been shown to possess numerous biological activities as well as other natural pigments (Langner & Rzeski, 2014). It appears to be more stable than other natural dyes in extreme situation. Although this pigment have potential as a natural brown colorants to substitute for synthetic browned-dyes (Ohe et al., 2017), the prime problem is that how to isolate it from real foods and model system efficiently to meet commercialization.

There are a large quantity of by-products that more or less have underutilized melanoidins, such as coffee grounds (Arya et al., 2022; Jiménez-Zamora et al., 2015), distilled spent grain (Lynch et al., 2016; Yang et al., 2019) and sugarcane molasses (Kaushik et al., 2018). This brown-colored dye needs to be isolation and purification prior to further application. Whereas, it is of great difficulty to choose a appropriate method as a result of its different structures in various systems. Melanoidins usually behave as anionic hydrophilic polymers. Most melanoidins existing in solid material can be extracted

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by water. However, the long time consuming and low recovery rate limit its widely use. Hence, For improving the extraction yields, some organic solvents as ethanol have been added to assist to extract. Apart from water maceration, sedimentation and enzyme-assisted methods are also applied in this pigment extraction. The conventional means still have disadvantages that can not be neglect. For this reason, focusing mainly on acquiring new technical approachs to couple with the traditional methods may be a promising alternative route.

In recent years, gradually, several emerging non-thermol techniques such as ultrasound-assisted extraction (UAE) (Ordóñez-Santos et al., 2021), microwave-assisted extraction (MAE) (Vinatoru et al., 2017), subcritical fluid extraction (SbFE) (Zhang et al., 2020), supercritical fluid extraction (SFE) (Uwineza & Waskiewicz, 2020), high hydrostatic pressure extraction(HHPE) (Scepankova et al., 2018) and pulsed electric field extraction (PEFE) (Kumari et al., 2018) have been carried out to enhance the extraction rate of bioactive compounds. These innovative techniques simply emit some kinds of energy performing on destroy the cell wall (Nirmal et al., 2021). Because of their prominent act in making time and organic solvents consumption fall off as well as increasing yield, researchs on optimizing process parameters and mechanism of extraction will be a hot topic. However,about melanoidins extraction, few studies have reported adopting these techniques. This review exploring the recent literature regarding the feasibility of emerging extraction methods and as a new potential natural brown pigment.

2 The chance of melanoidins

It is well-known that the appearance of items is a critical factor which may decide the passion of purchase of consumers. These colors are predominantly caused by artificial colorant.It's not just visually appealing,but also a signal to tell foods quality and avoid toxic or spoiled objects (Amorim et al., 2022). With the increase of consumers' awareness of health,searching for novel pigment sources is a issue that urgently need to be settle. Through unremitting efforts of researchs,natural colorants such as, carotenoids,anthocyanins betalains, and chlorophylls have been employed to produce various colors including red (Ozkan et al., 2022), orange, yellow, purple, and green (Santos & Bicas, 2021). However, in the case of brown colors,to date,only few available natural brown dyes have been reported. So,it gives rise to great interest for industrial to search for new brown pigments. What's more,a major breakthrough is also needed by researchers with respect to the applicability of brown colorants. There are some industries facing a shortage of novel brown pigments. Mixing natural and synthetic dyes may reduce the usage amount of non-healthy pigments (Brudzyńska et al., 2021).

1)Foods and beverages

At present,a large number of the natural brown pigments are obtained from different parts of plant, most of which are shells of seeds or fruit (Jin et al., 2018). Currently,caramel and cocoa colorants that account for the largest proportion in brown-colored dyes are the most employed in food and beverage factories. Although they have excellent stability,through further assessed,long-term consumption of these pigments are associated with to an increased risk of cancer. In addition,the content of hazardous heavy metal outweighs the beneficial elements.Based on this phenomenon, the researchers find that the existence of ammonium compounds can lead to the formation of 4-methylimidazole(4-MEI) during the manufacture process of caramel colorant.The U.S.National Toxicology Program(NTP) demonstrated 4-MEI does present a risk of cancer (Smith et al., 2015). Therefore, the recommended average dietary intake(ADI) varies in different ages and countries and every regulations must be more strict than European Food Standards Authority (EFSA) opinions (Sengar & Sharma, 2014). Even though there are clear regulations about a fitting range,several manufacturers do not take this clause into account in order to make interests.So in beverages and foods industries,searching for novel pigments that can meet consumers' demands is a future trend.

2)Cosmetic

Nowadays,due to the popularity of natural cosmetics,consumers pay more attention to the raw materials which obtained directly from nature.in addition,natural components are not only less sensitive to skin than chemically synthesized ones,but also may have various biological activities (Lourenço-Lopes et al., 2021; Morocho-Jácome et al., 2020).

pigments,which impart color to objects,can make cosmetic more attractive. Besides fragrance, the color of the products is one of the key criteria during cosmetics purchasing.In many western countries,there is no doubt that a growing number of people are obsessed with tanning,especially for young people. Food dyes without cytotoxicity and mineral colorants are usually used in cosmetics to cater consumers' expectations. However,if the exposure time is too long,most of them can exert irritation to skin and then influence physical health. It's reported that the addition of black ink of cuttlefish can increase the color intensity,covering capacity,spreadability (Brudzyńska et al., 2021). Hence, if products of various brands want to keep competitive in the market,manufacturers have to develop products with natural,multi-functional,harmless and effective characteristics.

3)Pharmaceutical

In pharmaceutical industry,drugs with more therapeutic effects and less side effects enable patients to convince.In addition to the effect,the color of medicine also plays an irreplaceable role in some respects (Pérez-Ibarbia et al., 2016). Firstly, It can color the capsules with an easily distinguished appearance that may mislead those senior patients who can not read the prescription clearly to drug abuse. Secondly,from a business perspective,color choices is one of the indispensable factors of realizing own brand effect and product identity in the pharmaceutical industry. Furthermore, it can prevent counterfeiting. Thirdly, it may also have a positive affection on the treatment effect because of the psychological effect (Mohd-Nasir et al., 2018). However, these pigments almost are made by a chemical reaction, its safety often set off panic among consumers. Although natural dyes may are beneficial to body, addressing the stability problem and complex toxicity evaluation are a precondition for subsequent application.

4) Textile

Although Synthetic dyes are well-established in a vast number of textile factories, a large number of investigations have certified these pigments as a major polluter of clean water,as it introduce many toxic chemicals that are non-healthy to body (Kumbhar et al., 2019). Some literature had reported coloring textiles with pigments produced by the Maillard reaction (Mongkholrattanasit et al., 2021; Ohe & Yoshimura, 2014). Therefore, for contamination control and meantime, color strength, color fastness and bio-functions of these pigments need to be testified whether be in accord with commercial criterion.

There is a gap in natural brown dyes supply. However, The introduction of Melanoidins may alleviate this problem. Historically,there seems to be a shift about perception of melanoidins over the last years. At first, they are treated as a sort of inert and antinutritional substance (Mesías & Delgado-Andrade, 2017). Later, the researchers found that these compounds are mainly responsible for accepted aroma,color and texture in thermally treated food.In following experiments,some biological activities concerning antioxidant are also reported in coffee and its by-product melanoidins. Also, some reviews underlined that the isolation of melanoidins might be a active ingredient added to food which promote health. Nevertheless,the literature related to the correlation between color and melanoidins have been rarely investigated. Up until now,its chemical structure is still an unsolved mysteries due to complexity of the reaction process. But a lot of researchers still be dedicated to study of structure, Wang observed a persuasive intermediate structure with 74 Da in vinegar, coffee and model melanoidins by dissociation using $NaBH_4$ (Wang et al., 2021).

At present, caramel pigments are the most accepted antioxidant colour additive used in bakery formulation. But this class of pigments has too many sugar which may lead to serious health issues, like obesity and cardiovascular disease. Furthermore, melanoidins may be an alternative that generated in commonly heating process. What's more, based on a large amount of scientific data, melanoidins play an important role in different food systems. In addition to these properties,an interesting probability is guessed for the near future: their potential use as a brown pigment that may meet the demands of some professions such as pharmaceutical, textile and cosmetic.

3 Color development

Melanoidins are intricated, nitrogen brown pigments produced by the Maillard reaction (MR). they have a maximum absorption at the wavelength of 420 nm. Some studies have already revealed that color formation is responsible for the third stage of Maillard reaction,where unsaturated carbonyl group and amines condense and forms high molecular weight compounds,called melanoidins. A several of reports, however, stated that there also have low molecular weight fractions (Starowicz & Zieliński, 2019).

Much efforts on exploring the formation mechanism of chromophore and its structure had been exerted by researchers. the mechanism of color formation chiefly involved aldol condensation, aldehyde-amine polymerization and formation of heterocyclic nitrogen compounds had been proved (Lund & Ray, 2017). After, the major formation mechanism of LMW Colored Maillard reaction products (< 500Da) were summarizd into several processes shown as Figure 1. Moreover, The structures of these LMW colored compounds have been identified by imitated experiments (Figures 2a- 2j) (Murata, 2021).

However, Brudzynski & Miotto (2011) find a striking difference between unheated and heated honey samples in color, which was positively correlated with the concentration of

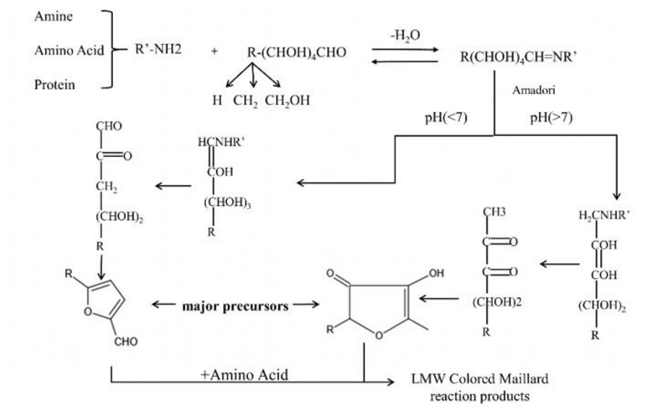

Figure 1. Predominant formation mechanism of LMW Colored Maillard reaction products.

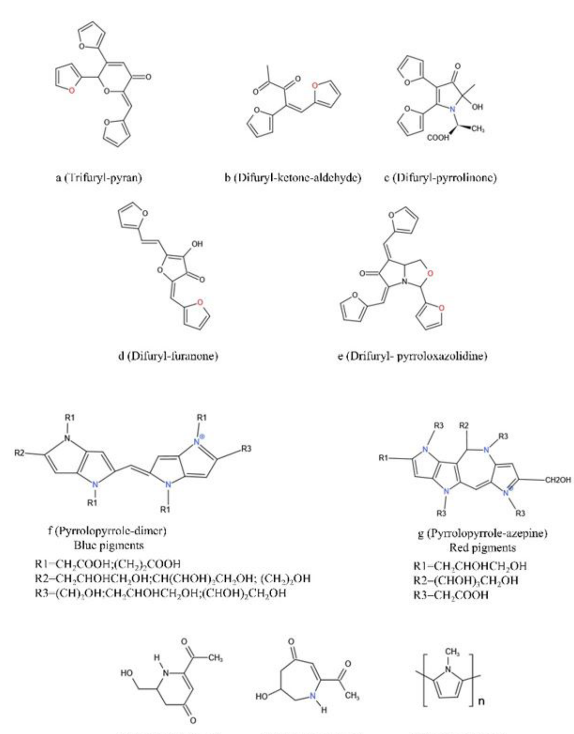

Figure 2. Some LMW chromophoric compounds (a-Trifuryl-pyran, b-Difuryl-ketone-aldehyde, c-Difuryl-pyrrolinone, d-Difuryl-furanone, e-Drifuryl-pyrroloxazolidine, f-Pyrrolopyrrole-dimer, g-Pyrrolopyrrole-azepine, h-Acetyl pyridinone, i-Acetyl azepinone, j-Pyrrole polymer).

melanoidins. Moreover,as the molecular weight increases, brown intensity increases too. In real foods, in terms of proportion, HMW fractions are much higer than LMW fractions. Like coffee, sweet wines, roasted malt and roasted cocoa beans, it has been demonstrated the brown color of these foodstuffs is predominantly caused by polymers of HMW melanoidins. Also, the MW of melanoidins depends on temperature,heat-up time and types of reducing sugars and amino acids. In model system, Kim & Lee (2008) mixed glucose with fructose-amino acids in temperature of 100 °C for 2 h, observed that produced mainly LMW colored polymers.

Moreover, Zhang (Mongkholrattanasit et al., 2021) investigated the color kinetics of Maillard reaction by three types of models and used L* (brightness), a* (red), and b* (yellow) to analyze color changes. Changes in pH result in the formation of melanoids containing different chromophores and conjugated systems,in addition,a rise in temperature would dramatically increase the intensity of browning together with a decrease in L*, a remarkable decrease in (b*), and a shift to (a*).

Consequently,industries may produce different molecular weight of melanoidins according to their own needs by controling different influencing factors,such as temperature, heating time,concentration of the sugar and amino acid, pH and water activity. Briefly, as the reaction time and temperature increase,the total carbon content increases,thus promoting unsaturated as well as color intensity. What's more, before the application, all types should be subjected to relevant detection experiments to ensure to reach the related hygiene and safety standards.

4 Biological activities of melanoidins

If it works well in some industries,its healthy and unhealthy biological activities should be studied.

4.1 Cytotoxicity

Diaz-Morales et al. (2021) observed that bakery product melanoidins were friendly to both Caco-2 and HUVEC cells at the concentration of 25, 50, 100 and 200 μg/mL, which refer to highest intake western diet. Nevertheless,although HUVEC cell viability has a modest fluctuation in 100 and 200 μg/mL, it is not enough to certify whether they are cytotoxic.So the following researchers would be dedicated to evaluate this change. However, it has been reported that the melanoidins from glucose-asparagine have an adverse impact on enzymatic activity of trypsin (Ibarz et al., 2009). Moreover,the greater the concentration of melanoidins is,the higher the enzyme inactivation is.

In conclusion, in high doses,melanoidins may display a slight Genotoxicity and cytotoxicity, but below the threshold, they do not pose physical threat to humans. Therefore establishing a dose range applied in different industries is an objective for subsequent experiments. No matter what industry it applies to, it should be in the condition that are harmless to human body.

4.2 Antioxidative activity

The positive antioxidative effects of melanoidins are just what the cosmetic industry needs most. So far, a lot of literature have already showed that melanoidin fractions in model or food systems have varying degrees of antioxidant activity. In vitro,such as vinegar (Liu et al., 2017a, 2016; Verzelloni et al., 2010), coffee (Tagliazucchi et al., 2010), bread-crust (Pérez-Burillo et al., 2020), dark beer (Tagliazucchi et al., 2010), biscuit (Patrignani et al., 2019), honey (Brudzynski & Miotto, 2011), coffee silverskin (Tores de la Cruz et al., 2019) and roasted cocoa (Oracz & Zyzelewicz, 2019). A great deal of studies demonstrated that melanoidins play a crucial role in antioxidant protective on lipid peroxidation (Yang & Gao, 2021) and gut (Pérez-Burillo et al., 2020). In vivo, Valls-Belles et al. (2004) confirmed that the model glucose-glycine melanoidins could safeguard rat hepatocytes against Doxorubicin-induced oxidative stress. Though the specific ingredient that act as a protective antioxidant are not yet clear, melanoidins may be still considered as a future antioxidative colorant applied in cosmetic section.

4.3 Antimicrobial activity

Goulas et al. (2018) studied the potential antimicrobial activity of Commandaria sweet wine melanoidins and found least inhibitory concentration of melanoidins is 5 mg/mL for three bacterial (Listeria-monocytogenes, Salmonella-enterica and Escherichia-coli). Interestingly, compared to low molecular weight melanoidins fractions,hihg molecular weight fractions with darker color possess better antimicrobial ability against Escherichia Coli. In addition,concerning antibacterial mechanism of these compounds,three diverse mechanisms accounting for this activity had been put forward (Rufián-Henares & de la Cueva, 2009). Melanoidins are known as anionic material, so metal cation can chelate them to achieve bactericidal effect; in second case,through chelating siderophore-Fe^{3+} complex some bacterial strains may have,which could weaken virulence of pathogenic bacteria; and, Finally, melanoidins at high concentrations can get rid of Mg^{2+} outside the cell From a business perspective, this biological activity of melanoidins may received much attention in producing antimicrobial pigments applied to textile dyeing because of the popularity of antibacterial cotton fabrics in recent years. Antibacterial cotton may keep skin from allergic reactions which caused by certain germs (Ben Fadhel et al., 2012). Furthermore,industries bosses may take melanoidins into account, it might be an alternative fabric dye.

4.4 Prebiotic activity

Prebiotics,an indigestible food component that beneficially affects the host by selectively stimulating the growth and activity of one or a few colonies of bacteria, thereby improving the health of the host, are a dietary supplement. Bifidobacteria and Lactobacilli are the most typical and well-known (Al-Sheraji et al., 2013). Borrelli & Fogliano (2005) initially simulated the hindgut environment in vitro and noted that bread crust melanoidins could be used as carbon and nitrogen sources and promote the growth of bifidobacterium.

Another research conducted by Jiménez-Zamora et al. (2015), also found that coffee spent grounds (CSG) and coffee silverskin (CS) showed the same prebiotic activity as bread crust. Recently, Nesreen (Aljahdali et al., 2020) carried out a experiment in vivo observed the intestinal probiotics of four experimental groups(consume melanoidins-rich malts ranged from 25% to 100%) rats had a significant increase by comparison with the control group. What's more,group with the highest intake displayed a most fierce increase. So consuming melanoidins amounts may be positively correlated with the growth of prebiotic. These studies suggested melanoidins have a considerable potential to be prebiotics.

More and more food and beverage brands cast their sights on functional food market because acclimating this trend is likely to attract more consumers (Hurtado-Romero et al., 2020). Commercially, it is estimated that the global prebiotics market is going to grow around 12.7% by 2025, which may bring a profit of approximately U$ 10.55 billion (Mano et al., 2018). In the past several years,diverse alternatives producing prebiotic components are being explored, particularly by using by-products. CSG and CS melanoidins exactly conform to this demand. Annually, according to incomplete statistics, after producing coffee, there will be more than 2 billion tons of by-product such as CSG and CS globally. Furthermore if food or beverage industries add them into foodstuff or beverage instead of caramel pigments, it would make a big deal of profits for those companies.

4.5 Antihypertensive activity

Hypertension is a clinical syndrome characterized by increased systolic and/or diastolic arterial blood pressure (systolic and/or diastolic blood pressure) (systolic pressure ≥ 140 MMHG and diastolic blood pressure ≥ 90 MMHG) and accompanied by functional or organic damage to the organs of the heart, brain and kidney. Many studies have revealed that one of the primary pathogenesis is an overactive renin-angiotensin-aldosterone system (RAAS). Moreover, researchers also discovered the activity of angiotensin converting enzyme (ACE) is a key factor during the entire RAAS blood pressure control system (Qian et al., 2019). Obviously, inhibiting ACE activity directly or indirectly might be a simple and effective therapeutic way.

In many foods and by-products,Melanoidins have a certain inhibitory effect on ACE. Rufián-Henares & Morales (2007) verified that food melanoidins (coffee,sweet-wine and beer) have indeed ACE-inhibitory activity via in vitro experiments and found those LMW compounds connected memelanoidins by non-covalent bonds are one of the contributors to inhibitory effect. In the meantime,the inhibition rates of different roasting degrees were also compared. According to the data obtained, maximum inhibition rate manifesting in the highest degree of roasting group. As well, various kinds of beer and wine melanoidins were studied. Similarly, Yang et al. (2019) reported that melanoidins of distilled spent grain (DSG)--a main by-product of baijiu brewing have ACE-inhibitory activity. By means of ultrafiltration, DSG melanoidins are classified into six molecular weight range (< 3 kDa, 3-10 kDa, 10-30 kDa, 30-50 kDa, 50-100 kDa, > 100 kDa). Melanoidins (3-10 kDa) are more effective in ACE-inhibitory activity.

A series of studies have proved that some food or beverage-derived melanoidins are shown to ACE-inhibitory activity. In a word, this indicated that melanoidins may be capable of lowering blood pressure in human body. Nowadays,young generation are gradually becoming candidates for hypertension due to overweight or induiging in high-salt diets. However, there is hardly few literatures about animal experiments on ACE-inhibitory activity. From the perspective of sustainable development strategy, DSG melanoidins deserved to be further studied. If some melanoidins work well, using these compounds might be not only improve the appearance of the tablet, but also make a enormous progress in global pharmaceutical industry.

4.6 Other biological effects

Early research by Hideo (Kamei et al., 1997) evaluated that whether melanoidins extracted from miso and soy sauce have a effect which can effectively block the growth and explored which period of cell growth cycle melanoidins affect. The results shows the suppression rates for both AGF cells and HCT-15 cells were up to 86.3%,98.0% respectively at the concentration of 100 μg/mL. Moreover, by culturing cells,they also found these melanoidins are likely to hamper S, G2, and M phase to prolong the tumor cell growth cycle. Thereby, this suggested that miso and soy sauce melanoidins may have Anticarcinogenic activity. LMW coffee melanoidins fractions were proved to have antiadhesive properties and prevented Streptococcus mutans (S. mutans) from saliva-coated hydroxyapatite beads. This is the cause of tooth decay. So it was proposed LMW coffee melanoidins have anticariogenic activity.

All the biological activities mentioned above may draw much attention and have a huge opportunity to be a novel natural pigment. Its participation may reduce the risk of adding caramel, make the medicine more effective to human body and produce more foods with different kinds of function. Thereby, future studies should exert much more efforts on extraction and isolation methods.

5 Extraction and isolation methods of melanoidins

Melanoidins,a kind of mixed macromolecule with complex structures and different degrees of polymerization,have strong hydrophilicity and are easily soluble in water and insoluble in organic solvents similar to most of other pigments. Based on this,the main extraction methods of melanoidins reported in literatures generally include water extraction, precipitation, adsorption,solution extraction and enzymolysis. However, due to the particularity of its structures, this is already a normal step that adding a small amount of NaCl (2 mol/L) into extracting solution. This operation can remove carbohydrates, protein, polyphenols and other macromolecular substances form the skeleton of melanoidins. At last, the obtained crude melanoidins need to be purified by some approaches,including ultrafiltration (Yang et al., 2019), Gel chromatography (Mikami & Murata, 2015), macroporous resin adsorption (Wang et al., 2008), size exclusion chromatography (Wang et al., 2021) and reversed-phase high performance liquid chromatography (RP-HPLC) (Mikami & Murata, 2015). These listed ways may used in combination at the process of extraction. What's more, the optimal choice of methods should be based on different food raw material. Table 1 briefly summarizes the most common approaches in the literature and their advantages and disadvantages.

Table 1. Main extraction methods of melanoidins.

Extraction Methods	Principle	Advantages	Disadvantages
water extraction	Some types of melanoidins that are soluble in water; Suitable for solid food materials	-Environment -friendly,non-toxic	-Low yields, -time-consuming
Precipitation extraction	Most types of melanoidins are insoluble in organic solven; Suitable for liquid food materials	-Compared with water extraction,melanoidins have less impurity	-Melanoidins inside the materials and cells may be inadequately extracted. -the concentration of organic solvents is too high to denature protein
Adsorption extraction	It is usually combined with water extraction and precipitation; Eluent: ethanol	-Large amount of adsorption -selective -save time	-A large number of optimization experiments are required to determine the most suitable resin,such as flow rate, time, elution rate, pH and so on.
solvent extraction	Extracting melanoidins of low polarity; methanol and ethanol are commonly considered as extractors.	-better effect on low polarity -fully extraction	-poor effect on large polarity -time-consuming
Enzyme extraction	Some melanoidins linked with protein and carbohydrate can cause low yields.The addition of enzymes can break down these large molecules to assist extract.	-efficient -high yields	-have more impurities

5.1 Water Extraction

Water Extraction (WE) is a common method for melanoidins extraction.It is very easy to operate and more appropriate for extracting water-soluble melanoidins from solid food material. Many researchers have studied melanoidins extraction using the WE. Mariana (Argirova et al., 2013) and Wang et al. (2019) both mixed coffee with hot water (90 °C) to extract water-soluble melanoidins, then filter through a bouchard funnel or filter paper after cooling and filtrate was degreased with dichloromethane. Actually,water extraction is widely used in the extraction of melanoidins from coffee. Nevertheless,a study conducted by Shiqi Yang et al. (2019) use water and sodium hydroxide solution to isolate DSG melanoidins.

While water extraction have the advantages of nontoxic and environmental, low extraction rate and long time consuming can not adapt to the speed of research. Moreover, nonpolar and water insoluble melanoidins are almost impossible to be extract.

5.2 Solvent Extraction (SE)

Due to polar and non-polar characteristics of melanoidins, Water extraction alone could not efficiently extract LMW fractions from beer and coffee. Thereby, when extracting, organic solvents are often added as extractors. Also, more and more solvent extraction methods have been reported in the literature. in the experiments of Suzuki et al. (2020), several extractors had been tried, such as water, methanol, ethyl acetate. But it turned out that acetonitrile was the best extractor. Another research carried out by fernando (Nunes & Coimbra, 2007), three methods (ethanol aqueous solutions, immobilized copper chelating chromatography and anion exchange chromatography) are developed to isolate HMW coffee melanoidins. A total of six melanoidins were obtained and their chemical composition was found to be different.

At present,from the related literature, researchers preferred ethanol solutions. Although SE has a high extraction efficiency for the components with low polarity, it is insufficient for the components with high polarity. Secondly, similar to water extraction, a single extraction is not sufficient for the extraction of melanoidins inside food materials, including cells and molecules, which not only takes a long time, but also affects the final results.

5.3 Precipitation extraction

The precipitation method have a characteristic of selectivity. Usually, this approach uses organic solvents as an extractor to precipitate the melanoidins.In published papers of Liu et al. (2017b) and Guo et al. (2012), ethanol and acetone were used to extract the melanoidins in coffee and soy sauce respectively. Subsequently, the precipitation obtained by filtration are freeze-dried.sometimes, this protocol also combined with the water extraction. Despite this method can reduce impurity contents and enhance the purity of product,the concentration of organic solvents is too high to lead to irreversible degeneration of protein structure in melanoidins.In addition,the most obvious limitation is that organic solvents are toxic to human body and not friendly to environment.

5.4 Adsorption extraction

Adsorption methods are generally sorted into two categories: chemical adsorption and physical adsorption. But in the process of extracting melanoidins,physical adsorption is more common than chemical adsorption.In the research of Echavarria et al. (2013). The researcher passed the diluted solution which contains model melanoidins through a glass column filled with active carbon and followed by extracting with Pyridine aqueous solution. Similarly, melanoidins from beer was isolated by macroporous resin.

Adsorption method utilizes the advantages of adsorption materials,such as large adsorption capacity,good selectivity, high adsorption rate, time saving and better stability, to extract or isolate melanoidins. Although this method is more efficient than other methods, a large number of authors are reluctant to apply it to melanoidins extraction. Since the chemical structure of melanoidins is not clear,the melanoidins from different food raw material also present varying degrees distinctions. Therefore, it is necessary to conduct a lot of optimization experiments before extracting different kinds of melanoidins which refer to adsorption material selection, pH and temperature.

5.5 Enzyme extraction

Melanoidins is a kind of polymer mixture with complex structure, which also exist in the form of protein complex. When extracting protein melanoidins, enzymatic digestion can be used to release the components in the protein structure. Cynthia (Helou et al., 2016) and Alves & Perrone (2015) used a certain concentration of streptompsin E phosphate/TrIS-HCl buffer for enzymatic digestion of bread crumbs and crust respectively, The supernatant containing hydrolysate was then ultrafilted using ultrafiltration membranes with different retained molecular weights, and last the obtained components were freeze-dried. However, enzymatic digestion is still time-consuming, can only dissolve part of the polymers, resulting in inadequate extraction.

6 Emerging non-thermal processing and its future application in melanoidins extraction

Time consuming, one of the defects of extraction methods mentioned above, may be a biggest barrier to industrial large-scale extraction. More recently, however, non-thermal processing for food has been focused upon by virtue of its excellent properties.

In recent years, the technology of extraction and separation of active ingredients in food has been developing towards improving product yields, increasing extraction efficiency, reducing the use of organic reagents and reducing the destruction of active ingredients (Tran et al., 2022). Under this background, SFE, HHPE, PEFE, UAE, MAE and other non-thermal processing techniques are favored by the industries, showing a great development potential.The extraction process for non-thermal technology is shown in Figure 3.

Ultrasonic wave is an acoustic wave with a frequency rate of 20~50 kHz. It has good directivity and strong penetration ability. The combined effects of cavitation, vibration, crushing and agitation can effectively destroy cell wall membrane, promote the release of bioactive compounds, increase mass transfer and achieve the process of extracting intracellular content (Ordóñez-Santos et al., 2021). Except for Chinese researchers, almost no researchers have tried UAE to assist in extracting melanoidins. However,according to the experimental result, UAE showed high performance with respect to shortening extraction time and increasing yield compared to control group. Therefore, UAE may have a great boost on extracting melanoidins from food raw materials.

Analogous to the advantages of this method of extraction, Such as the destruction of cell wall membrane, promote the release of biological active substance. The prospect of some non-thermal processing techniques in the assisted extraction of melanoidins can be predicted. However, there are few reports on the application of these kind of techniques in the extraction of melanoidins, which belongs to a new field.

HHPE is a new non-thermal processing technology, which uses water as the medium of pressure transfer to enhance material transportation.In the process of extraction, ultra-high hydraulic pressure can reach each parts of the material instantly and evenly. At this point, a large pressure difference between the inside and outside of the cell membrane is formed, which promotes the solvent to enter the cell through the broken membrane and improves the mass transfer rate (Dhiman et al., 2021). Zhao et al. (2019) studied the extraction of high-molecular-weight melanoidins from Black Garlic using HHP. Data showed that HHPE improved the extraction efficiency and moderate parameters (treatment

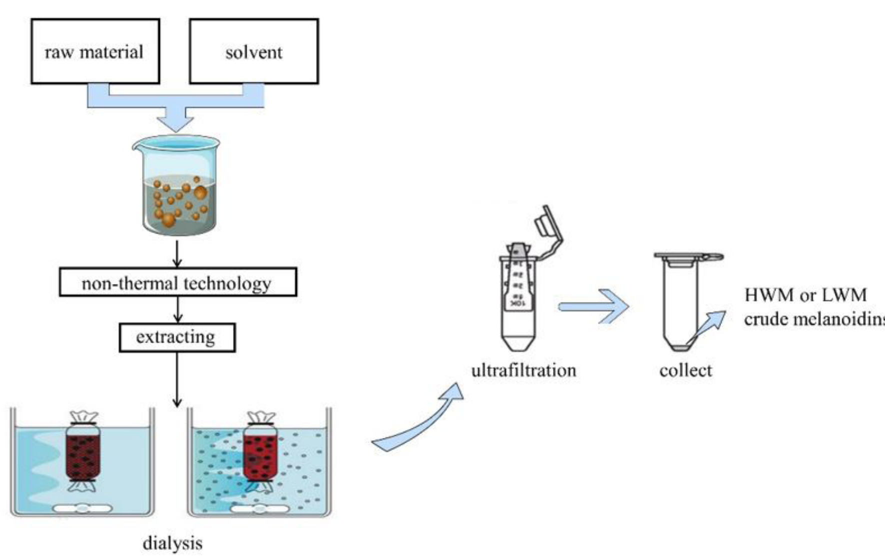

Figure 3. The flow-process diagram of melanoidins extraction.

pressure and holding time) can significantly increase the amount of total phenols and flavonoids. Moreover, ACE, PTB-1B, and trypsin inhibitory activities were also augmented.

SFE is a new, clean, efficient and green separation technology, which integrates the advantages of two chemical unit operations (distillation and liquid-liquid extraction) and easily diffuses through solid materials (Zhang & Du, 2022). In addition, Supercritical carbon dioxide is usually employed as a ideal solvent to assist extraction.In the experiment of Maran et al. (2014), researchers used supercritical carbon dioxide extraction method to extract anthocyanins and phenolic compounds from dried ginger fruit.The optimum extraction conditions were found through optimization, The obtained total anthocyanin content and phenol content were 1143.051 ± 1.58 mg/100 g and 231.28 ± 0.76 mg/100 g, respectively. Compared with other extraction methods, supercritical fluid extraction technology had higher extraction rate and shorter extraction time.

PEFE is based on the application of instantaneous pulses with high electric field intensity (0.1 ~ 50 kV/cm) at room temperature. It is a non-thermal extraction method that can improve the extraction rate of plant bioactive components because it can disintegrate cell membranes in plant materials (López et al., 2009). López et al. (2008) studied the effects of 5 and 10 kV/cm pulsed electric fields on the extraction of phenolic compounds from grapes during fermentation. The results showed that the anthocyanins extracted from grape skins treated with pulsed electric field at room temperature increased from 835.29 mg/L to 965.02 mg/L (5 kV/cm) and 1056.06 mg/L (10 kV/cm). The total phenol content increased from 70.65OD280 nm to 83.1OD280 nm (5 kV/cm) and 87.7OD280 nm (10 kV/cm).

Furthermore, there are a lot of data reported in literature on pigment extraction employing emerging non-thermal techniques. These non-thermal processing technologies can shorten the extraction time, increase the extraction efficiency and improve the purity of the extract to reduce the loss of activity of the extracted ingredients and environmental pollution.

While these novel technologies have many advantages, there is no doubt that the introduction of new equipment will increase the cost, and the need to periodically inspect equipment for safety further expand the cost, making scale and industrial application a challenge. On the other hand, as a growing number of consumers are more inclined to buy green, natural, high sensory quality products, investors can choose the appropriate methods and equipments according to the characteristics of the pigment to reduce the cost. Further investigations are needed to develop cheaper equipment, safer and more tailored processes.

In the future studies of melanoidins, With the further study of it, it is an inevitable trend to use these non-thermal processing technologies or in combination with other technologies for the extraction and separation of melanoidins in food, and it will also show a bright application prospect in the field of extraction and separation. All in all, any new technology or process has its own limitations and needs to go through a long development process and a lot of scientific research and practice.

7 Conclusion

It is possible that Melanoidins as a natural pigment applied to cosmetic,textile,pharmaceutical food and beverage. This compound is not only abundant in source but also has many special biological activities. Each year,a large number of by-products containing melanoidins are produced worldwide such as DSG, CSG and CS, which have a detrimental effect on environment. Industries can properly exploit the color of melanoidins in these by-products to replace artificial pigments. Moreover,they can produce multiple functions commodity by adding melanoidins. But it is necessary to carry out professional performance tests of pigment before industrial application. The main challenge for industrialization of melanoidins is its isolation, however, Its application prospect is worth exploring new extraction methods. Therefore, in this context, The combination of the conventional methods and the emerging non-thermal methods may be the research hotspot in the future.

Enthical approval

This article does not contain any studies with human or animal subjects.

Conflict of interest

The authors have no conflict of interest to declare.

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