

Progress on the melanoidins produced by the Maillard reaction of fermented food and traditional Chinese medicine

Guang-Zhen Cao¹, Si-Yi Zhang¹, Yao-Song Yang¹, Qing He¹, Xin-Xian Song¹, Fei Long¹, Teng Peng^{1*}

¹ School of Pharmacy, Chengdu University of Traditional Chinese Medicine, Chengdu, China.

*Corresponding to: Teng Peng. School of Pharmacy, Chengdu University of Traditional Chinese Medicine, No.1166, Liutai Avenue, Wenjiang District, Chengdu, Sichuan, China. E-mail: pengteng@cducm.edu.cn.

Competing interests

The authors declare no conflicts of interest.

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Abbreviations

FMs, Food-borne melanoidins. TCM, Traditional Chinese Medicine.

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Abstract

FMs (Food-borne melanoidins) are brown high molecular weight polymers formed by the Maillard reaction between carbohydrates and nitrogen-containing compounds during the processing of food or Traditional Chinese Medicine (TCM), and are widely found in food-borne products such as TCM concoctions, bakery, brewing, soy sauce, ferment and other food-borne products. FMs not only have a variety of biological activities, such as antioxidant, antibacterial, immunomodulation, regulation of intestinal flora, etc., and can change the color, aroma and taste of food. The diversity of its components has become a research hotspot at home and abroad in recent years, with a wide range of application prospects. Therefore, this paper summarizes the existing information on FMs at home and abroad, mainly describes their preparation process, physicochemical properties, structural characteristics and functional activity research progress. Typical FMs, such as coffee, biscuits, wine and soy sauce in daily food, and Polygonatum, Perilla oil, Black ginseng, and Red jujube in T, were highlighted. Summarising the current status of research between the chemistry and pharmacodynamics of relevant FMs and presenting challenges and future recommendations for melanoidin research. In future research on FMs, one should pay more attention to basic research, especially isolation and purification and generation mechanisms, to further demonstrate the biological activity of FMs in vivo and in clinical trials. Thus, the potential value of its existence is deeply exploited to meet the needs of technology, production and health.

Keywords: Food-borne melanoidins, Physical and chemical properties, Structure, Functional activities, Application prospects

Background

FMs (Food-borne melanoidins) are brownish high molecular weight polymers formed by the Maillard reaction between carbohydrates and nitrogen-containing compounds during food processing [1]. Food thermal processing is as old as man's discovery of fire. The main sources of FMs are related to the processing of daily food and TCM, which statistically account for about 6-40 percent of the dietary intake of human beings. During thermal processing, many chemical reactions and physical transformations occur during food thermal processing, and the Maillard reaction is important for food quality, safety and health effects [2]. The reaction is a non-enzymatic browning reaction with three main stages, the initial stage refers to the nucleophilic addition reaction between reducing sugars and amino compounds to generate Amadori products, the products undergo rearrangement, dehydration and other reactions to generate iminosugars and other unstable intermediate products; The middle stage refers to the condensation and cyclisation of iminosugars with other nitrogen-containing compounds to produce a variety of aromatic compounds, such as pyrazines, pyrazoles, thiazoles, etc., which can provide the aroma and colour of foods; The later stage is when the aromatic compounds undergo polymerisation, condensation and other reactions with other nitrogen-containing compounds or on their own to produce brown high molecular weight polymers, i.e., FMs [3].

FMs are summarised as existing in two main aspects, previous studies mainly focused on one aspect, i.e., nigrosomes produced from fermented foods, while this paper adds nigrosomes produced from the processing of TCM, analyse and describe the compositional variations of melanoidins from the perspective of TCM. The key feature of FMs is that they impart a distinctive flavour and texture to the food, with a prominent brown or dark brown appearance (Figure 1). The processing of food, such as common coffee [4], biscuits [5], apples [6], soy sauce [7], etc. The melanoidins are not only involved in the change of the colour of the food, but at the same time affect the odour and the way of storage of the food; On the other hand, it mainly exists in the processing of TCM, as we all know, most of the raw products of TCM are accompanied by a variety of foreign substances such as soil, or accompanied by toxicity, and the raw products directly into the medicine will stimulate the throat, and even have toxic side effects, in the application of the necessary processing before the Chinese herbal medicine composition, colour and lustre in the concocting process of qualitative and quantitative changes, which will enhance the

biological activity of the TCM or change the action of the drug tends to be [8]. For example, in the concoction process of Polygonati rhizoma with wine added during the production process, the colour of Polygonati rhizoma and yellow wine changed from yellowish-white to brownish-brown after steaming, and the decrease in the content of polysaccharides, the main component, was closely related to the continuous production of melanoidins [9]. Perilla oil produced melanoidins during microwave pretreatment to further improve the quality and flavour of the oil [10]. Red jujube by temperature and humidity control ripening into black jujube, black jujube compared to red jujube is not only higher nutritional value, and can make up for the defects of low antioxidant activity of red jujube, to further broaden the field of red jujube deep processing [11]. During the preparation of Carbonized Rehmannia root, a Maillard reaction was produced to obtain the product melanoidins, which was used as an indicator for the optimisation of the preparation process, and the mechanism of Rehmannia charcoal's efficiency and toxicity reduction was also explored [12]. It can be seen that the role of melanoidins is very crucial for the in-depth study of food safety and the mechanism of TCM concoctions. As of 2024, this paper searched the Web Of Science for the keyword "melanoidins", and the literature data of the past ten years are shown in Figure 2. The studies on melanoidins mainly include wastewater hydrolysis (19.5%), coffee (26%), and chemical synthesis models (18.75%), with the three being the most prevalent and widely studied. The main FMs described in this paper account for about 35.75% of the total, of which about 6% are TCM, and daily food products contain bread (6%), wine (6.5%), vinegar (2%), soy sauce (2%), and a review of other food groups (12.75%). It can be seen that studies on more food-borne aspects of melanoidins are more limited, and food studies are still mostly in coffee, lacking a specific summary of FMs. Therefore, the aim of this paper is to provide a comprehensive summary of the current status of FMs. This paper reviews the preparation process of FMs and systematically collates the existing research data on the physicochemical properties, structural characterisation and biological activities of FMs. With special reference to the production of melanoidins in TCM and insights at the level of herbal concoction mechanisms. The aim is to increase the reader's knowledge of FMs and to provide a reference for further research on the use of melanoidins in food safety and human health.

Process for the preparation of FMs



Figure 1 Typical foods and TCM with brown or black appearance

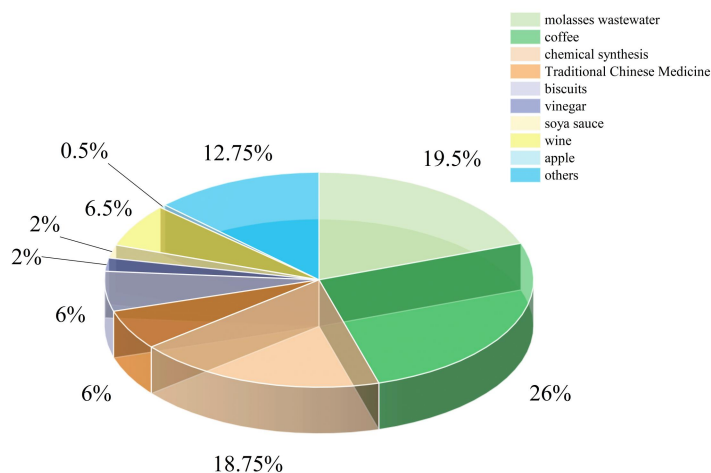


Figure 2 Percentage of literature from different sources of melanoidins in Web Of Science

Table 1 Main stages and specific conditions for the production of different FMs

Name of food	Raw materials	Stages of melanoidin production	district	Reference
nattō	Soya, rice	38-44°C, fermentation for 6 months	Japan	[13]
soybean paste	soybean	28-30°C, fermentation for 40 days	South Korea	[14]
fermented apple	Apple	High temperature (60-90°C); High humidity (50-90%)	China	[6]
yellow wine	Rice, corn, millet, wheat	30°C, fermentation 5-7 days; 15°C, fermentation 30-60 days	China	[15]
soya sauce	Soybeans, wheat	14-30°C, high salt solid state fermentation 3-6 months; 45-55°C, low salt solid state fermentation 15 days	China; Japan; South Korea	[7]
coffee	coffee beans	Shallow: 180 °C baking 90s, 10min30s (235 °C a burst); Medium: 14min27s (200 °C two burst); Deep: 18min5s (235 °C three burst)	China	[16]
black bean	Soybeans, black beans	Trichoderma: 20°C, fermentation more than 6 months; Aspergillus type: 30-35 °C, fermentation 40 days; Root mold type: 36 °C, fermentation 36 h; Bacteria type: 30-32 °C, fermentation 3 months	China	[17]
(grape) wine	grapes	Expose the grapes to sunlight and heat them up to 50-55°C when the daytime temperature is >35°C.	Italy; Spain	[18]

The preparation process of FMs is currently mostly traditional, i.e., the naturally occurring Maillard reaction during processing, such as baking, brewing, fermentation, etc., which has the advantages of low cost, simple operation, stable products, etc., but the disadvantages are the long reaction time, the reaction conditions are not easy to control, and the quality of the product is not easy to guarantee. The main concoctions that may produce melanoidins in the processing of TCM are the nine-steaming-nine-explosive, wine, vinegar, and calcination systems, Honey system, etc., because most of them are carried out under high temperature and high humidity conditions, which is conducive to the process of the Maillard reaction, most of the current research on melanoidin is mainly in food, and there are few in TCM, therefore, melanoidin in TCM holds a greater prospect for research, and more energy needs to be invested in exploring and researching.

Physico-chemical properties of FMs

Solubility

The solubility of melanoidins is related to the size of the polymer and the nature of the reactants, and different sources of melanoidins have different aqueous solubilities, which also provide a basis for the choice of isolation and purification methods. Melanoidins in soy sauce and liqueur have been reported to be moderately water-soluble, whereas those in stout are highly water-soluble, and proteinaceous melanoidins usually have high molecular weights and are mostly insoluble [19]. Therefore, it can be deduced that most of the melanoidins present in fermented soya bean products are probably water insoluble and require organic reagents for their extraction. In addition, when low molecular weight compounds (monosaccharides and amino acids) are embedded in polymers, the solubility of the resulting high molecular weight melanoidins increases, and another hydrophobic melanoidins are converted to hydrophilic melanoidins under certain conditions, and their solubility and light-transmitting refractive indices also increase [20]. It can be seen that the solubility of melanoidins is not only related to the raw material and its processing method, but also closely related to its extraction and purification method.

Stability

The melanoidins are mainly affected by light, temperature, PH and metal ions. The absorbance of Aspergillus-type tempeh-type melanoidins solution decreased significantly when the temperature was higher than 80°C, PH > 7, and Fe³⁺ and Al³⁺ were added, which shows that fermented tempeh-type melanoidins is suitable to be stored in a low-temperature, acidic environment, and avoiding the interference of metal ions, such as Fe³⁺, as much as possible [21]. In the stability study of ripened wolfberry-like melanoidins, > 40°C made the melanoidins extremely unstable; The retention was only 40% at high concentration of H₂O₂ and remained above 70% at Na₂SO₃ with less effect [22]; After the addition of black garlic melanoidins to food preservatives, sodium benzoate had a certain colour enhancing effect on the melanoidins, while potassium sorbate had a minimal and insignificant effect on the stability of the melanoidins [23], and another study on the addition of black garlic melanoidins to food additives showed that there was almost no change in the overall stability of the melanoidins, but both potassium sorbate and sodium benzoate with a mass fraction of 4%-8% had a certain effect on colour enhancement [24]. Similarly, soy sauce is unstable under light (100000 Lux), high temperature (> 80°C) and addition of Fe³⁺ and Cu²⁺ [7]. In conclusion, the stability of melanoidins generated from different raw materials may vary, and the examination of stability is necessary for the storage and in-depth study of melanoidins.

Chelation of metal ions

The melanoidins is an anionic hydrophilic polymer, which can form ligands with metal cations and participate in metal chelation (CuCl₂, CrCl₃, FeCl₃, ZnCl₂, PbCl₂, etc.), and has been mostly known as metal chelating agent in recent years, and studies have shown that the chelating performance of melanoidins on metal ions is closely related

to its antioxidant and antimicrobial activities, and it also showed potential value [25]. The ability of honey-like melanoidins to form complexes with Pb²⁺, Zn²⁺, Ni²⁺, Cu²⁺, Fe²⁺, Cd²⁺ and Co²⁺ improves its antioxidant capacity [26]. The binding efficiency of the sweet wine type of stout to iron was higher than that of the different types of beer (pilsner, ale and dry stout) type of stout, but lower than that of the coffee and model types of stout. Compared to barley, coffee and stout-based melanoidins, vinegar-based melanoidins showed higher Fe²⁺ chelating capacity but lower haemoglobin binding capacity, and furthermore, it has been shown that an important parameter for examining the iron chelating capacity of melanoidins is the type of sugar, and glucose was found to be more effective than lactose [27]. Overall, the chelating ability of the different source classes of melanoidins with metal ions was good, with most of them having the strongest chelating ability with Fe²⁺.

Molecular mass

It was found that the immediate precursors of melanoidins are α -dicarbonyl compounds and also the most important intermediates in carbohydrates, which are closely related to the formation of melanoidins and molecular weight size distribution [27]. The molecular weights of the coffee-based melanoidins were mainly distributed in 2.94 × 10⁴ kDa and 4.56 × 10⁴ kDa, with proportions of 27.5% and 72.5%, respectively [28]. Honey-based melanoidins are high molecular weight brown compounds with a minimum molecular weight of 66 kDa and a maximum of 235 kDa, while honey-based melanoidins show peroxy radical scavenging activity [29]. The molecular weights in soy sauce range from 3000 to 55000 Da and 10330 to 137596 Da, respectively [30]. In summary, melanoidins are large molecular weight mixtures with a wide range of molecular weight sizes, which is one of the reasons why the specific structure of melanoidins is difficult to characterise.

Methods for the analysis and detection of FMs

Scanning electron microscopy (SEM)

Scanning electron microscopy (SEM) is the observation of the surface morphology of samples, which is a new type of electron-optical instrument developed rapidly in recent years. It is widely used in the structural characterisation of samples and in the identification of authenticity due to its quick and simple method and high resolution [31]. The morphology of coffee melanoidins varies with different molecular weights due to the fact that the sugar hydroxyl groups are connected by non-covalent bonds and form intermolecular hydrogen bonds, which changes the appearance of the polymers, and the morphology of different molecular weights of melanoidins is different, according to the molecular weight, the morphology is as follows: > 100 kDa: irregular flakes or strips; 50-100 kDa: smaller smooth flakes; 30-50 kDa: a large number of holes and irregular; < 30 kDa: flakes finely fragmented, with a variety of morphologies [28]. The malt-based melanoidins samples all showed a reticulated skeleton and spherical particle accumulation, which may be due to the unfolding of malt proteins and the disruption of non-covalent bonds during the roasting process [32]. SEM characterisation of the surface morphology of the different source classes of melanoidins can also reflect the differences in surface morphology for different molecular weights.

Elemental analysis

Elemental analysis (EA) is often used at the initial stage of structural identification to obtain the elemental composition and chemical shortest formulae of melanoidins. Yang et al [19] used an elemental analyser to determine the proportions of C, H, O, and N in the reaction product of glycine and glucose (1:1) as 53.42 %, 4.38 %, 4.26 %, and 37.61 %, respectively. The chemical shortest formula of malt melanoidins obtained after baking at 250°C for 40 min was C₁₈H₂₇O₁₁N. Eriko Suzuk [33] found the elemental compositions of C, H, and N in Japanese black vinegar (Kurozu) melanoidin to be 35%, 6.6%, and 4.4%, respectively, by elemental analysis. Elemental analysis has a wide range of applications and is a quick way of analysing the types

and percentage of elements commonly found in melanoidin, but has the disadvantage of being sensitive to only a small number of elements, the exact structure of which is unknown.

Spectroscopic method

Ultraviolet spectroscopy

The UV spectra of different molecular weight melanoidins in crystalline malt were similar at 200-800 nm, with the absorbance of the higher molecular fragments being significantly higher than that of the lower molecular fragments, indicating more chromophores. The absorption peaks of MW-3 are present in both the UV and visible regions, indicating its strong absorption properties [34]. Mariela Patrignani and Lucía del Sol González-Forte found in beer melanoidins that the absorbance at 294 nm was related to the presence of early melad reaction products and low molecular weight melanoidins, whereas the absorbance at 420 nm increased with the presence of high molecular weight melanoidins [35]. The higher the content of melanoidin, the stronger the structural cross-linking and the higher the absorption capacity. In addition, all the samples showed considerable absorption at 200-350 nm in association with unsaturated aldehydes and ketones or conjugated systems, indicating that melanoidins have $\pi-\pi^*$ electron leaps on C-C bonds, and $n-\pi^*$ electron leaps on C-C bonds for C-O and N-O bonds. In conclusion, UV spectroscopy is simple and quick to operate, and it is very easy to be used for the crude quantification of melanoidins, but melanoidins are a kind of polymer mixtures, and it is not possible to make a quantitative judgement on them.

Fourier infrared spectroscopy

Infrared absorption spectroscopy analyses the composition of substances and is often used to identify the structure of organic matter. The IR spectral characterisation of different classes of melanoidins is shown in Table 2. The functional groups of the compounds were identified by analysing the characteristic absorption frequencies of the important functional groups and qualitative and quantitative analyses were carried out. The infrared spectra of melanoidins eluted at different concentrations are similar to each other, and infrared spectroscopy is widely used in the structural identification of compounds because of its high sensitivity and scanning efficiency. However, since FMs are high molecular weight mixtures, the complexity of the elements and the composition can interfere with their infrared spectral peaks and cause bias in the results, so most of them need to be combined with other structural analyses.

Fluorescence spectroscopy

Fluorescence spectroscopy is a fingerprinting technique where different substances have different fluorescence properties. The fluorescence intensity of Yunnan small-grain coffee melanoidins was significantly different under different storage conditions, in which the fluorescence intensity was inversely proportional to the temperature in the range of 10~80°C; the fluorescence intensity of the aqueous solution of melanoidins with PH=5~10 was more stable; the fluorescence intensity of the aqueous solution of melanoidins stored in a sheltered place did not change significantly in 60 min ($P > 0.05$), and an increase of the time of exposure to light led to a significant decrease of the fluorescence intensity. The fluorescence peaks in the range of $\lambda_{ex} = 250-600$ nm, $\lambda_{em} = 320-700$ nm for different molecular weights of the coffee-based melanoidins, among which there is one obvious fluorescence peak at $\lambda_{ex} = 400$ nm, $\lambda_{em} = 480-490$ nm, which may be related to the presence of carboxyl groups, carbonyl groups, aromatic groups, alkanes, and other groups in the coffee-based melanoidins [40]. The fluorescence intensity of aqueous solutions of black liquor-type sperm decreases with increasing molecular weight. Low molecular weight (< 30 kDa) fluorescence value: 10000, high molecular weight (> 100 kDa) fluorescence value: 1444. The reason for this may be that the graded treatment depolymerises phenolic and amine compounds to produce small

molecules with rigid structures, which leads to an increase in fluorescence intensity, whereas there is a fluorescence burst in the darker colours of the high molecular weight components [29]. In summary, it can be found that melanoidins has certain fluorescence characteristics, and compared with ultraviolet spectroscopy, it has the advantages of high sensitivity and selectivity, but due to the complexity and uncertainty of the composition of melanoidins, a variety of substances interfering with melanoidins can not be accurately detected by the quantitative detection of the melanoidins.

Mass spectrometry (chemistry)

Mass spectrometry is a method that uses the trajectory of FMs in electric or magnetic fields to achieve their qualitative and quantitative properties. It is commonly used to combine two or more analytical and detection methods to obtain simultaneous isolation, quantitative and structural information on FMs, and it can avoid the limitations and deficiencies of a single method in order to improve the analytical and detection results of FMs. Commonly used mass spectrometry methods include electrospray ionisation mass spectrometry (ESI-MS), laser desorption ionisation mass spectrometry (MALDI-MS) and gas chromatography-mass spectrometry (GC-MS), of which GC-MS is widely used. Zhu et al [41] detected 50 melanoidins-like pyrolysis products from different colours of high-temperature dacquoise, with 50, 39 and 39 species in black, yellow and white quartz, respectively, and there were significant differences in the composition of the melanoidins-like pyrolysis products, with the melanoidins-like structure of black quartz being the most complex. The volatile components of Yunnan small-grain coffee were extracted by ultrasonic extraction with dichloromethane, and detected and analysed by GC-MS. 37, 45, and 46 volatile components were detected from light, medium, and dark-roasted coffee melanoidins, respectively, which were dominated by furoalcohols, furfural, furans, pyrazines, pyrroles, and phenolics, among which the contents of furoalcohols and furfural increased with the increase of the roast degree [16]. LC-MS can be used to directly characterise the structural composition of melanoidins. For lower molecular weight melanoidins, the structure can be resolved by liquid chromatography-electrospray ionisation-mass spectrometry (LC-ESI-MS), which was used to demonstrate that the structure of honey melanoidins contains hexose oligomers in the bound state, and sucrose, maltose, turpentine or maltotriose [29]. MALDI TOF-MS analysis identified a series of ionic peaks of Japanese black vinegar with a difference of 162.055 ($C_6H_{12}O_6 \cdot H_2O$) in m/z indicating a change in the length of the dextran chain. Significant signals in the dextran unit at m/z 500-600 indicate ionic peaks in the proteinaceous melanoidins fraction [42]. In summary, the mass spectrometry methods of melanoidins are various and convenient, among which gas phase-mass spectrometry (GC-MS) is more widely used. The other methods adopt ionisation or electrospray to decompose ions more efficiently, and qualitatively identify and quantitatively analyse small and medium molecules of melanoidins as well as volatile constituents, but their existence can only be matched with known compounds in the database, which is a certain limitation, and they are not able to detect new substances, while the other method of liquid phase-MS can detect non-volatile constituents. Another type of liquid chromatography-mass spectrometry (LC-MS/MS) can detect non-volatile components, but the molecular weight of melanoidins is large, which requires a higher degree of separation between melanoidins and other macromolecular substances.

Functional activity of FMs and their mechanisms

In our rapidly evolving modern society, there is a growing awareness of healthy eating, and the World Health Organisation, in its latest Healthy Eating Theme, explains that maintaining a healthy diet throughout the life course can help prevent various types of malnutrition and a range of non-communicable diseases and conditions. People's dietary patterns have changed along with social lifestyles, especially in today's diversified food processing,

Table 2 Infrared spectral characterization of different FMs

Names of melanoidins	functional group (chemistry)	Reference
Black garlic melanoidin	3400cm ⁻¹ -OH; 2927cm ⁻¹ -CH、-CH ₂ ; 1612cm ⁻¹ C=O、N-H、C-N、C-C、C-H; 1400cm ⁻¹ C-N; 1050cm ⁻¹ C-O、C-C、C-H	[23]
Stout melanoidin	3400cm ⁻¹ -OH、-NH、-CH、-CH ₂ ; -C,C-O; 1658cm ⁻¹ ,1542cm ⁻¹ ,1248cm ⁻¹ C-O (acidamideI)、N-H (acidamideII)、C-N, N-H deformation (acidamideIII) ; 1414cm ⁻¹ C-H; 1080cm ⁻¹ , 1000cm ⁻¹ C-O	[36]
Melanoidin from wine lees	3271cm ⁻¹ -OH; 2936cm ⁻¹ -CH、-CH ₂ ; 1679cm ⁻¹ acidamideI (C-O Expansion); 1438cm ⁻¹ , 1370cm ⁻¹ C-H; 1240cm ⁻¹ acidamideIII (C-N); 1150cm ⁻¹ , 1017cm ⁻¹ C-O-C、C-O-H	[37]
Sorghum Vinegar melanoidin	3415cm ⁻¹ -OH; 2958cm ⁻¹ -CH ₃ 、-CH ₂ ; 1724cm ⁻¹ C=O、-COOH, 1626cm ⁻¹ C=O、C=N1414cm ⁻¹ -CH、-CH ₂ ; 1200cm ⁻¹ , 1000cm ⁻¹ C-O-C;	[38]
Yellow wine melanoidin	3415cm ⁻¹ -OH; 2958cm ⁻¹ -CH、-CH ₂ ; 1618cm ⁻¹ C-N, C=O, C=N and N-H	[39]

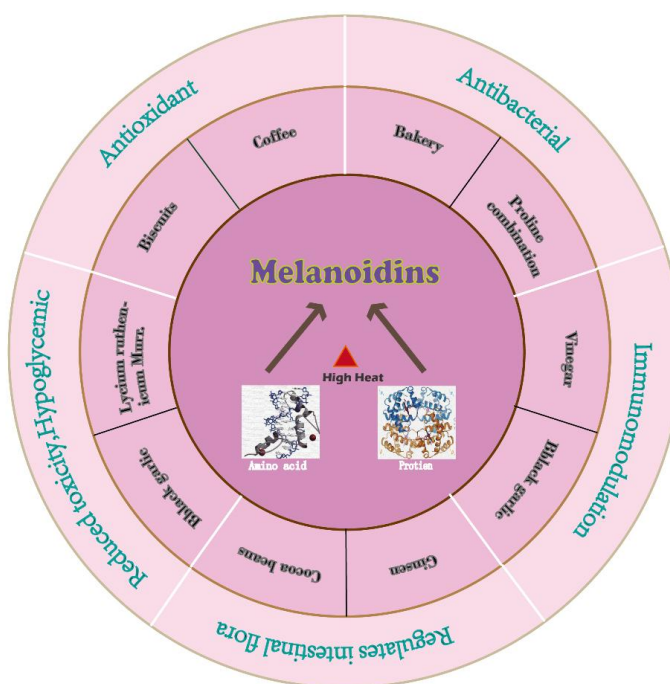


Figure 3 Some biological activities exhibited by melanoidins in FMs

and melanoidins, as common compounds present in food and TCM processing, have gradually attracted the attention of the society with their wide range of biological activities. The functional properties of melanoidins need to be further explored, and their dosage control ranges are crucial for a healthy diet. Melanoidins have a wide range of biological activities (Figure 3). The following section focuses on the antioxidant, antimicrobial, immunomodulatory and modulation of intestinal flora of food-borne analogues of melanoidins.

Antioxidant

FMs have strong antioxidant activity, scavenging free radicals, chelating metal ions and inhibiting lipid peroxidation. Free radicals

are harmful substances produced in the human body as by-products of metabolism leading to cancer and cardiovascular diseases, whereas melanoidins attenuate the effects of these free radicals and protect cells from oxidative DNA damage, and biscuits melanoidins fractions attenuate the oxidative stress in human HepG2 cells by enhancing antioxidant defences in cell culture studies, thus enhancing their antioxidant capacity [43]. Coffee melanoidins protect human hepatocellular carcinoma cells from oxidative damage by regulating glutathione levels, MDA formation and activation of antioxidant enzymes, and studies have shown that melanoidins account for up to 25% of the dry matter of coffee, thus they play an important role in the formation of coffee creamer, and further give coffee beverages their sweet and sour flavour [44].

Antibacterial

The antimicrobial properties of the melanoidins analogues were found to be better in various melanoidins analogues. Melanoidins in common bread showed the widest range of antimicrobial activity, and melanoidins successfully inhibited the growth of *Bacillus cereus* and *Bacillus shortis*. Baker's yeast melanoidins, as a natural antimicrobial agent, can play an effective role in the food process properties, and improve the shelf-life and safety of food products [45]. The melanoidins produced by combining xylose with phenylalanine or proline showed a wide range of antibiotic effects against various pathogens, including *Listeria monocytogenes*, *Bacillus cereus*, and *Salmonella typhimurium*, and since the antimicrobial effect of the melanoidins against *Listeria monocytogenes* was equivalent to that of the lacto-streptopeptide solution (350 IU/mL) [46], in the future development and research of the Chinese, we can expect the application of FMs as a novel food preservative.

Immunomodulation

The immune system is the host's tight defence mechanism to resist the invasion of antigens and maintain the body's homeostasis. In addition to bacteria and viruses, physiological and emotional fluctuations can cause disruptions in the body's immune system, and it is particularly important to maintain the homeostasis of the immune system. There has been increasing interest in how to improve the self-regulation of the immune system. Immunological analyses confirmed that the four subfractions obtained from the purified melanoidins of Shanxi old Chen vinegar showed a significant enhancement of cell viability, phagocytic activity, and secretion of nitric oxide, tumour necrosis factor, and interleukin (IL)-6 in RAW264.7 cells, and the mechanism of immunomodulation might be that the purified subfraction SAV-RP70-X not only enhances the aerobic glycolysis of macrophages, but also activates multiple receptors [47]. The significant increase ($P < 0.05$) in phagocytosis of melanoidins on mouse peritoneal macrophages, with higher phagocytic recovery space in males, presumed that females had higher drug resistance and that analogues had a better recovery effect on immunodeficient male mice. This result is consistent with the analysis of weighted data. It is widely recognised that the immune systems of males and females are different [48].

Regulates intestinal flora

The intestinal flora is rich in variety and large in number and usually resides in the gastrointestinal tract of humans, which is known as the second set of genetic code of human beings, and participates in the metabolic functions of the organism for the treatment of metabolic disorders such as obesity, and studies in recent years have shown that the relationship between intestinal flora and obesity is very close [49]. The melanoidins-like substance isolated from ginseng may inhibit choline metabolism by synergistically regulating the intestinal flora and the AMPK pathway, which not only significantly reduces the reduction of trimethylamine (TMA) and trimethylamine n-oxide (TMAO) levels, but also increases the content of short-chain fatty acids, thus regulating the intestinal flora [50]. The in vitro digestibility of bound phenolic compounds and the potential prebiotic activity of cocoa protein melanoidins have been demonstrated by studies that released polyphenols during digestion and produced short-chain fatty acids during in vitro fermentation [51].

Other research

With the continuous research, the rich bioactivities of melanoidins have been continuously discovered. Black garlic contains melanoidins that can attenuate toxicity and lower blood glucose, which restored ZEN (zearalenone)-induced adverse effects on zebrafish embryo development, including delayed hatching time, morphological

abnormalities, and neurodevelopmental deficits, attenuated cytotoxicity and significantly inhibited ZEN-stimulated apoptosis in zebrafish larvae, and the high-molecular-weight fluorescent fractions had a good α -amylase and α -glucosidase inhibition, and the inhibitory ability was positively correlated with the concentration, inferring that black garlic contains melanoidins that have the potential to block postprandial blood glucose elevation [52]. The residue after extraction in LBP contains melanoidins, which are important substances that can be used as environmentally friendly pigments in textile colouring [53].

Summary

With the promulgation of a series of health policies, people are paying more and more attention to the health field. As a kind of natural substance with various functional activities, FMs has a broad application prospect in the food industry and health field. FMs have been consumed as an important part of daily human diet and health. In the health field, FMs have gradually been found to be present in the process of concoctions, participating in a variety of chemical reactions, as well as being one of the components of concoctions that increase the effectiveness and reduce the toxicity of TCM. However, research on melanoidins has mainly focused on chemically synthesised models and bakery products, and little attention has been paid to processed TCM and fermented foods. This paper presents the first systematic review of FMs, especially the compilation of information on melanoidins in TCM, which enriches the sources of it. FMs are mainly produced during high temperature and high humidity, traditional fermentation, long-term storage, and Chinese medicine concoctions. Currently, due to the variety and complexity of structures, its isolation and purification is the most basic and challenging research on FMs. The understanding of the structure and specific components of melanoidins is still insufficient to further quantify the melanoidins and elucidate their mechanism, and its progress will play a great role in the promotion of melanoidins research and the development of the health industry of TCM.

This review helps one to grasp the current state of research on FMs and informs further research on melanoidins. In the future research could focus on the basic research on melanoidins and more in vivo and clinical trials are needed to demonstrate the health benefits of melanoidins. The final attempt is to obtain a controlled production of melanoidins, with selective formation, to maximise the health benefits of FMs.

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