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Yufa, S, Lin, L orcid.org/0000-0001-9123-5208 and Peiyu, Z (2021) Color Development Kinetics of Maillard Reactions. Industrial and Engineering Chemistry Research, 60 (9). pp. 3485-3778. ISSN 0888-5885

https://doi.org/10.1021/acs.iecr.1c00026

Colour development kinetics of Maillard reactions

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KEYWORDS: Maillard reaction, dihydroxyacetone; amino acids; colour development kinetics; browning intensity

ABSTRACT: Maillard reactions have been reported extensively. However, full colour development kinetics of Maillard reactions have rarely been studied in detail. This study systematically investigated the colour development kinetics of Maillard reactions. Thus, arginine (Arg), histidine (His) and lysine (Lys) were each reacted with dihydroxyacetone (DHA) using a simplified model system at different molar ratios, reaction times, pH and temperatures. Importantly, the browning intensity (at 450 nm) and full colour characteristics (within *CIE L*a*b** colour space) were measured and analysed in detail. Minitab® statistical software was employed to design factorial experiments and analyse the main and interaction effects. It was found, for the first time, that His and Lys reacted with DHA more rapidly than Arg and the difference was obvious with the increase of molar ratio and reaction time, reflected in the change of *b**. pH6.2 and higher temperature favoured the formation of deeper coloured products in AA-DHA, accompanied by reduced lightness (*L**), significant losses in yellow hues (+*b**) and shifts toward red hues (+*a**). The greatest browning intensities of Arg-DHA (A_{450}=0.63), His-DHA (A_{450}=1.12) and Lys-DHA (A_{450}=1.18) were achieved at molar ratio = 3, 72 hours, pH6.2 and 50 °C, with corresponding *L**, *a** and *b** values being 54.51, 14.03, 42.75; 48.26, 47.28, 13.59 and 43.35, 53.64 and 10.82, respectively.

1. INTRODUCTION

Maillard reactions occur in many agricultural, food and cosmetic products. In 1960s and 1970s, Maillard reactions took a centre stage when they became the basis of operation of sunless tanning products. Tanning has become an incredibly popular activity in Western countries, especially for young people, since a tanned skin is usually perceived as attractive and healthy. The most readily available method to achieve tanned skin is to expose skin to sunlight[1,2]. Unfortunately, this practice has many drawbacks and can cause harm to health. Indeed, many studies have reported that excessive ultraviolet (UV) radiation can damage the skin's DNA leading to faster aging of skin and even skin cancers, such as melanoma, squamous cell carcinoma and basal cell carcinoma[3,4]. Therefore, it is not surprising that there is a huge and growing demand for sunless tanning products, since these products not only provide skin with the sun-kissed look without exposure to strong sunlight, but also offer moderate UV protection at Sun Protection Factors (SPF) of approximately 2-5[5,6].

Dihydroxyacetone (DHA), a three-carbon sugar, is the main active ingredient in commercial sunless tanning products[7]. The chemistry of DHA tanning is similar to the well-known Maillard reaction (also known as nonenzymatic browning reaction), which has been extensively studied and used to control the colour, flavour, taste and texture in sugar-containing foods[8,9]. It is widely recognised that DHA can react with free amino acids (AA) derived from α-keratin in the skin's stratum corneum (SC) via Maillard reaction to form brown pigments known as "melanoidins"[10], as shown in Figure 1. In 1960, Dr Eva Wittgenstein of the Children's Hospital of University of Cincinnati discovered, by accident, that the splashed DHA darkened the skin while using DHA as an oral drug to assist children with glycogen storage disease[11]. Soon after, the first commercial self-tanning product was launched in the market and achieved great success immediately. In 1977, the US Food and Drug Administration (FDA) approved the DHA as the only legal tanning agent for external application in cosmetic products with a concentration of up to 15%[12].

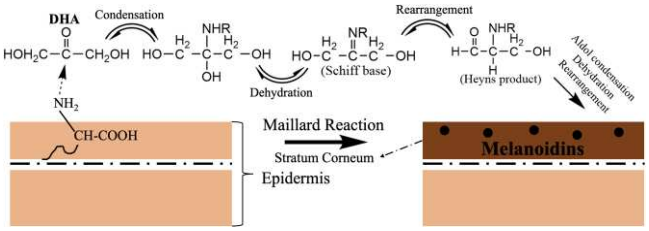

Figure 1. Proposed reaction of DHA with amino acids of stratum corneum

Since then, the roles of DHA in the tanning reactions have attracted considerable research attention. For examples, Pantini *et al.* introduced a perfluoropolyether phosphate as a new acidic agent to lower the pH and increase the stability of DHA[13]. Carnali *et al.* systematically studied the structure and property relationship of ethylenediamine derivatives as aids to increase the rate of tanning[14]. In addition, there have been a number of observations of

free radicals being involved in the production of melanoidins on skin. Buettner and co-workers detected the signal of the endogenous ascorbyl radical in mouse skin by electron spin resonance (ESR) spectroscopy[15]. Roger *et al.* investigated the *in vivo* formation of free radicals in mouse skin and found that this reaction was similar to its *in vitro* reactions with amines and amino acids[16]. Jung *et al.* reported that more than 180% additional radicals were generated in the DHA-treated skin by radical sun protection factor method during UV exposure[17].

In spite of the extensive studies on tanning reaction, the exact reaction pathways and chemical structure of melanoidins are still unknown due to the complexity of the reaction. In order to better understand the colour development of DHA, it would be necessary to study tanning reaction within suitable chemically constituted model systems rather than natural skins which are chemically invariably complex. It has been reported that arginine, lysine and histidine are abundant in the epidermal proteins of the SC[11,18]. However, there has been a lack of systematic study of the kinetics of their colour generating reactions with DHA. Hence, the study reported in this paper investigated reactions between these three AA and DHA in buffer solution. More specifically, the browning rates of DHA with AA were investigated under various reaction conditions, such as the molar ratio of DHA to AA, reaction time, pH and temperature.

The authors believe that understanding of the nature and kinetics of colour development would provide a facile route to studying Maillard reaction pathways, bearing in mind that the colour of a molecule is largely determined by the structure of the molecule. Nguyen and Kochevar reported their observation of the shift of the λ_{max} towards the longer wavelength region as Maillard reactions between DHA and AA within SC progressed[10]. However, no information on full colour characteristics were shared. Therefore, the work reported here quantitatively studied the full colour characteristics of the model solutions based on the change of their *CIE L*a*b** values as the reaction progressed under various conditions. Minitab® was used to design factorial experiments and analyse the experimental data obtained to study factors that have significant effects on the colour development kinetics. These findings not only provide a foundation for further study on the chemical structure of melanoidins, but also can be utilised as a basis to develop strategies to control and improve the tanning effect of DHA in sunless tanning products more efficiently.

2. EXPERIMENTAL SECTION

2.1 Chemicals

Dihydroxyacetone ($C_3H_6O_3$, 99%) was supplied by PZCussons (Manchester, England). L-Arginine hydrochloride ($C_6H_{14}N_4O_2{\cdot}HCl$, 98%) (Arg), L-Histidine hydrochloride ($C_6H_9N_3O_2{\cdot}HCl$, 98%) (His) and L-Lysine hydrochloride ($C_6H_{14}N_2O_2{\cdot}HCl$, 98%) (Lys) were purchased from Ajinomoto Inc. Hydrochloric acid (HC1, 36.5%), sodium acetate ($C_2H_3NaO_2$, 99%) and acetic acid (CH_3COOH, 99.7%) were supplied by Sigma-Aldrich Corporation. di-Sodium hydrogen orthophosphate dodecahydrate ($Na_2HPO_4{\cdot}12H_2O$, 99.1%) and sodium phosphate monobasic dehydrate ($NaH_2PO_4{\cdot}2H_2O$, 99.1%) were supplied by Fisher Scientific International Incorporation.

2.2 Preparation of buffer solutions

0.1 M acetate buffer and phosphate buffer solutions were prepared according to Table S1, with the pH values of buffer solutions confirmed using a 3051 Jenway pH Meter.

2.3 Ultraviolet-visible spectrometry

Ultraviolet-visible (UV-Vis) spectrometry was performed on a dual beam Varian Cary 100 UV-Vis spectrophotometer (Agilent Technologies), equipped with a xenon pulse lamp and scan software. The browning intensity of model reaction solution was determined at 450 nm using a quartz cuvette (10 mm, QS, Hellma). Each sample was analysed in triplicate, and the mean value are reported. Samples with the absorbance values in excess of 1.2 were diluted with distilled water before analysis.

2.4 Colour characterisation

The colour characteristics of reaction solutions were represented via *CIE L*a*b** (*CIELAB*), which is a colour space defined by the International Commission on Illumination (*CIE*) in 1976[19], that expresses colour as three values: L^* for the lightness from black (0) to white (100), a^* from green (−) to red (+), and b^* from blue (−) to yellow (+), shown in Figure S1, where chroma (C^*) and hue (h) can be represented by Equation 1[20]:

$$C^* = \sqrt{a^{*2} + b^{*2}} \qquad h = arctan\frac{b^*}{a^*} \tag{1}$$

Colour measurement involved pipetting the sample aliquot into a 1 cm polymethyl methacrylate (PMMA) plastic cuvette, and measuring the *L*a*b** values of the sample against a white background using a Datacolor CHECK 3 (Datacolor Inc., UK), with an 8° diffuse D65 illuminant and at a 10° observer angle, calibrated using a standard white and black plate. Each test was carried out in triplicate and the mean value is reported.

2.5 Experimental design

2.5.1 Selection of factors and their ranges of variation to study

The concentrations of DHA in sunless tanning products usually range from 1% to 10%[21]. To take the effect of DHA concentration into consideration, the molar ratios of DHA to AA were set at 1, 2 and 3, with the corresponding final concentrations being 0.3, 0.6 and 0.9 mol/L ($\approx$ 3%, 6% and 9%, respectively)[22]. It has been reported that DHA takes 3 - 12 hours to start tanning reaction with the stratum corneum of skin, and the ensuing darkening process continues for 24 - 72 hours[21]. The stratum corneum of human skin has a pH gradient from an acidic pH to a neutral

pH (4 - 7), and in most cases, it is slightly acidic with an approximate pH of 5.5[23]. In addition, the normal human skin temperature is around 36 °C, and it can usually tolerate higher temperatures upto 50 °C without being harmed[24]. Based on the above information, the following parameters and their ranges of variation were chosen for the study reported here:

- AA type: Arginine, Histidine and Lysine (3 levels)
- DHA/AA molar ratio: 1, 2 and 3 (3 levels)
- Reaction time: 24 hours, 48 hours and 72 hours (3 levels)
- Reaction temperature: 36, 43 and 50 °C (3 levels)
- pH of reaction mixture: 4.4, 5.0, 5.6, 6.2, 6.8 and 7.4 (6 levels)

2.5.2 Design of factorial experiments

pH and temperature are believed to play crucial roles in Maillard reaction. In order to minimise the number of experiments and to focus on the effects of pH, temperature, the optimum molar ratio and reaction time on the rate of browning reaction were first sought through a set of full factorial experiments (DOE). Thus, using Minitab® software, a set of 27 experiments were design as shown in Table S2. Based on the optimised reaction conditions obtained from this set of experiments, the influences of pH and temperature on the rate of browning reaction were further emphatically studied through a single-factor control variable method.

2.6 Preparation of AA-DHA reaction solutions

The three model reaction solutions were denoted as Arg-DHA, His-DHA and Lys-DHA, respectively. These AA-DHA solutions with different molar ratios and reaction times were prepared and shown in Table S3. Each AA-DHA solution sample was dissolved in 10 mL 0.1M acetate buffer solution of pH5.0 in a plastic test tube, sealed and allowed to react at 36 °C for 24, 48 and 72 hours, respectively. Then, AA-DHA solutions with different pH values were prepared according to Table S4. Each AA-DHA solution sample was added to 10 mL 0.1M buffer solution in a plastic test tube, sealed and allowed to react at 36 °C for 72 hours. Finally, Table S5 shows details of AA-DHA solutions in 10 mL 0.1M phosphate buffer (pH6.2) for the study of the effects of temperature on the rate of browning reaction.

3. RESULTS

3.1 Effects of AA type, molar ratio and reaction time on the tanning reaction of AA-DHA

Figure 2 shows the effects of AA type, molar ratio and reaction time on the DHA tanning reaction. The corresponding data are summarised in Table S6. As shown in Figure 2(a), the browning intensity of the same AA-DHA shows an upward trend with the increase of the molar ratio and reaction time. In particular, increases in the molar ratio and reaction time both significantly promote the A_{450} values of His-DHA and Lys-DHA, while it has very little effect on that of Arg-DHA. The highest A_{450} values of Arg-DHA, His-DHA and Lys-DHA are achieved with 0.18, 1.51 and 1.16, respectively, at the molar ratio of 3 and the reaction time of 72 hours. This indicates that His and Lys react more rapidly with DHA than Arg, along with faster reaction rate at increased molar ratio and reaction time. In addition, these conclusions are further confirmed by factorial plots shown in Figure 2(c) and 2(d). As exhibited in Figure 2(b), b^* value shows a similar upward trend for the same AA-DHA as the change of the A_{450}, suggesting that the colour is getting increasingly yellow with the increase of molar ratio and reaction time. The highest b^* values of Arg-DHA, His-DHA and Lys-DHA are 0.49, 60.11 and 36.29, respectively. However, a^* varies in different AA-DHA systems with the increase of molar ratio and reaction time. At the same time, these changes have little effect on the value of a^*, suggesting that b^* value plays a major role in the browning intensity of reaction at pH of 5.0 and temperature of 36 °C. Images of these systems are shown in Figure S2.

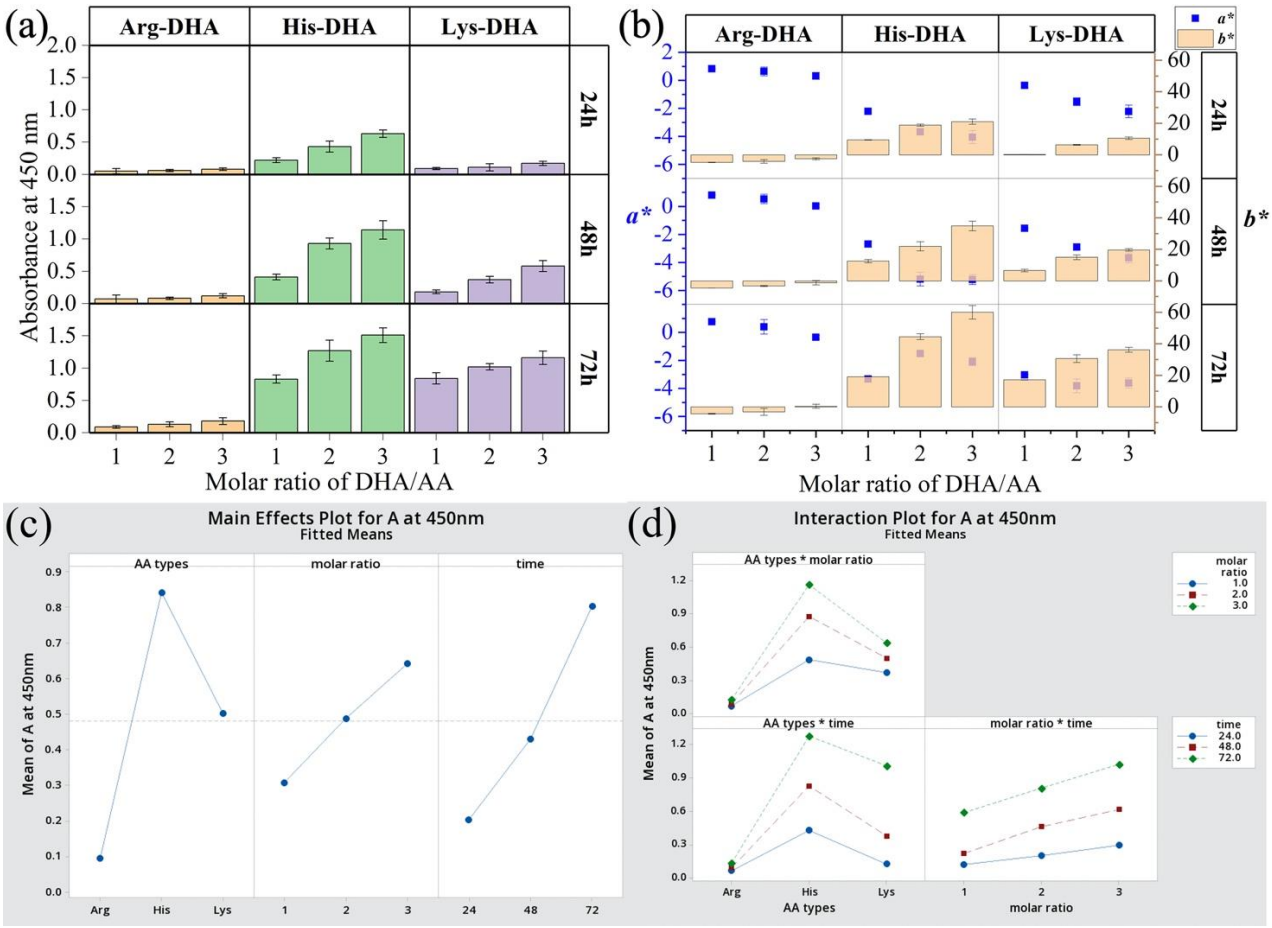

Figure 2. Effects of AA type, molar ratio and reaction time on browning intensity of AA-DHA solutions: (a) Absorbance at 450 nm, (b) a* and b* values, (c) Main effects, (d) Interaction plots.

3.2 Effects of pH on the tanning reaction of AA-DHA

Figure 3(a) shows that the increase in browning intensity as a function of pH is not linear, but all three AA-DHA systems show similar trends. In general, the A_{450} increases first and then declines as the pH increases from 4.4 to 7.4 (A_{450} values of these samples were obtained after they were diluted 10 times). The A_{450} values of Arg-DHA, His-DHA and Lys-DHA peak at pH 6.2 at 0.26, 0.91 and 0.98, respectively, suggesting that weak acidic condition is beneficial for DHA and AA to produce chromophores. Besides, the browning intensity of His-DHA and Lys-DHA are always much higher than that of Arg-DHA solution. It is worth noting that A_{450} of His-DHA is always higher than that of Lys-DHA at lower pH (<6.2), but the reverse is true at higher pH ($\geqslant$ 6.2). At the same time, the difference of A_{450} between His-DHA and Lys-DHA is not obvious at higher pH. These results are in accordance with the work of Nguyen et al., who reported that lysine and histidine reacted more rapidly with DHA than other amino acids and had a greater reaction rate at pH7 than that at pH5[22]. The effect of pH on the a^* and b^* of AA-DHA can be observed in Figure 3(b). Similar to the variation in the browning intensity, a^* and b^* values both go up first and then down with the increase of pH. The highest a^* and b^* values of Arg-DHA and His-DHA are reached at pH6.2 at 1.43, 12.63 and 15.84, 64.13, respectively. However, only the a^* value of Lys-DHA is the highest at 25.17 at pH6.2, and the b^* value is 45.35. Besides, the browning intensity of Lys-DHA is higher than that of His-DHA, indicating that a^* value plays a dominant role in the browning intensity when b^* value is maintained at a high level. The relationship between these values and colour is also summarised in Figure 3(c), where changes in a^* and b^* values corresponding to colour variations can be observed. Images of these samples and relevant data are shown in Figure S3 and Table S7, respectively. In addition, in order to discover whether the compositions of buffer solutions would affect the colour characteristics of tanning reactions, Arg-DHA, His-DHA and Lys-DHA mixtures were prepared in pH6 acetate- and phosphate-based buffer solutions, respectively, and their colour characteristics measured. It can be seen, from Table S8, that although the components of the buffer solutions are different, each system exhibited almost the same colour characteristics at the same pH value.

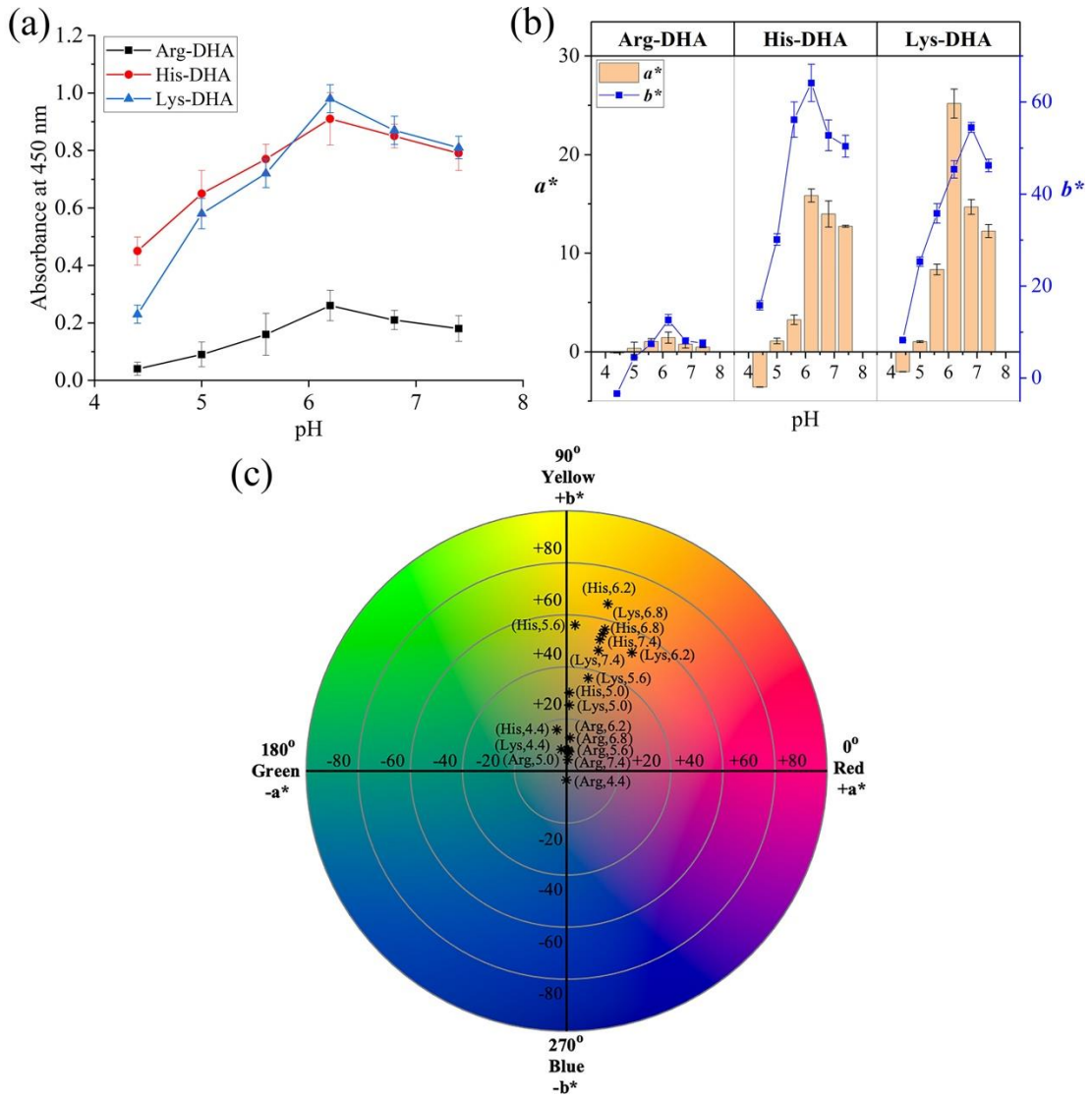

Figure 3. Effects of pH on browning intensity of AA-DHA solutions: (a) Absorbance at 450 nm, (b) a* and b* values, (c) CIELAB colour chart.

3.3 Effects of temperature on the tanning reaction of AA-DHA

The effects of temperature on the browning intensity of AA-DHA are shown in Figure 4(a). A dramatic increase in A_{450} for all AA-DHA is observed when temperature increase from 36 to 50 °C, following an almost liner relationship (A_{450} values of these samples were obtained after they were diluted 40 times). The browning intensity of His-DHA and Lys-DHA are consistantly significantly higher than that of Arg-DHA at the same temperature. The highest A_{450} of Arg-DHA, His-DHA and Lys-DHA are achieved at 50 °C at 0.63, 1.12 and 1.18, respectively. Figure 4(b) shows the variation in a^* and b^* with the increase of temperature. The a^* value of all AA-DHA shows a similar upward trend, while the trends of variation of the b^* value of His-DHA and Lys-DHA are opposite and that of Arg-DHA first increases then declines. The a^* and b^* values of Arg-DHA, His-DHA and Lys-DHA are 14.03, 42.75, 47.28, 13.59 and 53.64, 10.82 at 50 °C, respectively. These phenomena can be seen intuitively in Figure 4(c), where the browning process is achieved by significant losses in yellow hues ($+b^*$) and shifts toward red hues ($+a^*$). Images of relevant solution samples and corresponding data are exhibited in Figure S4 and Table S9, respectively.

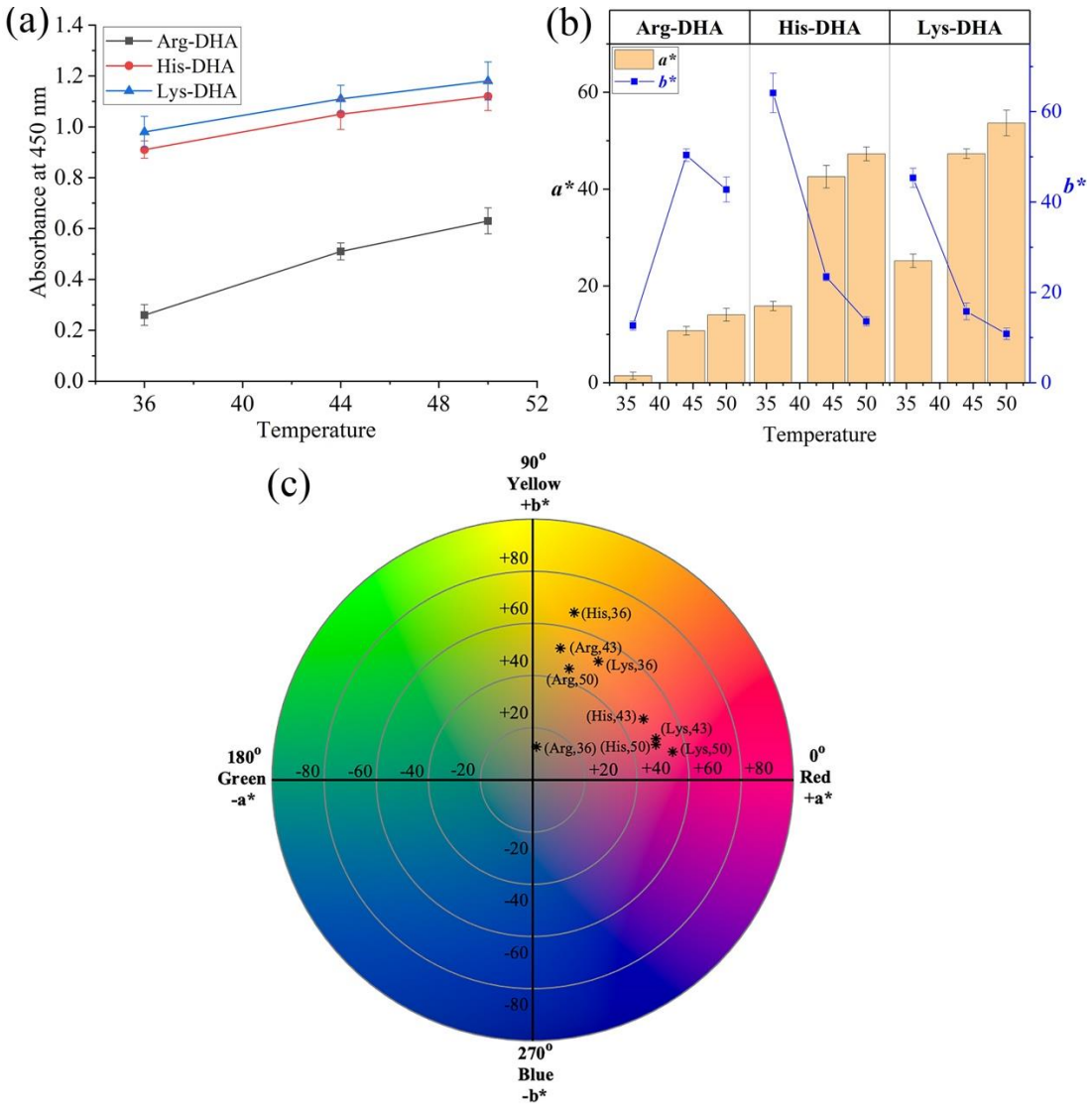

Figure 4. Effect of temperature on browning intensity of AA-DHA solutions: (a) Absorbance at 450 nm, (b) a* and b* values, (c) CIELAB colour chart.

4. DISCUSSION

The reaction of DHA with AA produces complex polymers containing visible-light absorbing chromophores, known as "melanoidins". The melanoidins possess a highly conjugated double-bond structure and are similar to the natural melanin in the deeper skin layers[14]. Although the absorbance at 420 - 450 nm has been widely used to evaluate the browning intensity of Maillard reaction in the food field, it is difficult to quantitatively describe the characteristics and changes of colour, especially in the dermato-cosmetic research[25]. The tristimulus colorimetry is a better and recommended approach to describe the skin colour by referring to the L^*, a^* and b^* values[26]. Meanwhile, the extent of browning can be better understood when described using a^* and b^* [27].

In terms of AA type, Arg, Lys and His are representative due to their high contents in the SC of skin. Besides, compared with other acidic and neutral amino acids, they are all basic amino acids, which is believed to provide the source amine and have a higher reactivity with DHA. In particular, Arg has been widely recognised as the most reactive amino acid towards DHA and being responsible for most of tanning effect on human skin, because it has the highest content with 15.9% in the human epidermis and contains two amino groups[28]. However, the results obtained through the studies reported in this paper revealed different observations. It is discovered that at 36 °C and pH5.0, Arg-DHA is almost colourless and does not develop a stronger colour with the increase of molar ratio and reaction time. Even under the other same reaction conditions studied, for example, investigating the effects of pH and temperature on the tanning reaction, the browning intensity of Arg-DHA is much lower than that of His-DHA and Lys-DHA. It is believed that such a phenomenon is due to the difference in the molecular structures of these AAs. As shown in Figure 5, the pKa_2 (α-NH_2) values of Arg, His and Lys are similar, but their pKa_3 values are significantly different, thus producing different isoelectric points (pI) at

10.76, 7.59 and 9.74, respectively. When their molar concentrations are the same at a given pH below their pI, His with low pI has relatively more unprotonated amino groups, facilitating nucleophilic attacks on the carbonyl groups of DHA molecular to form more melanoidins[14]. At the same time, the imidazole group of His is beneficial for the formation of melanoidins with a larger conjugated system, producing a darker colour. At 36 °C and pH5.0, the colours of His-DHA and Lys-DHA are mainly yellow. In addition, as the molar ratio and reaction time increase, the colour of all AA-DHA gradually deepens. However, the colour of tanning reaction is not brown but yellow, which is reflected in the change in b^* value.

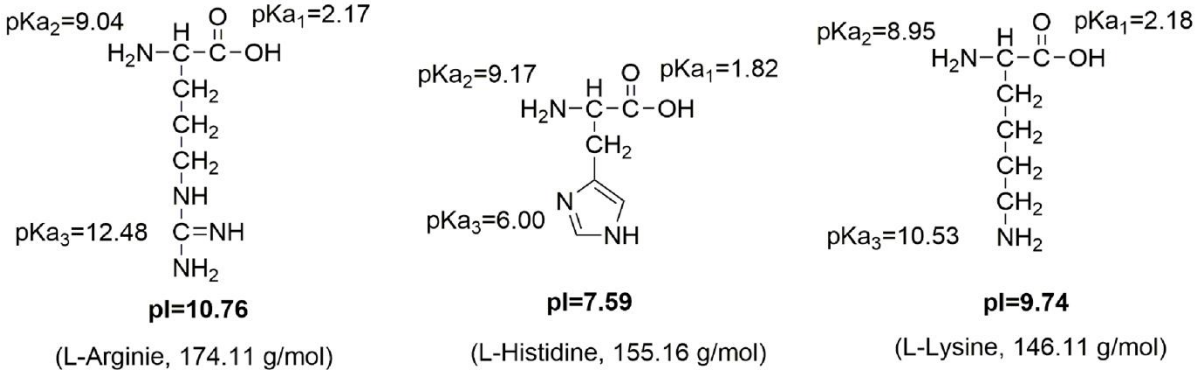

Figure 5. Structure, protonation constants and pI of three basic amino acids

Previous studies have shown that pH plays a crucial role in the Maillard reaction of food, but few have systematically investigated its effect on the tanning reaction between DHA and AA[29,30]. Figure S3 shows that the change in pH causes a clearly observable difference in the colour of the solution. The browning intensity of Arg-DHA, His-DHA and Lys-DHA all increase sharply as the pH increases from 4.4 to 6.2, because more unprotonated amino groups are released to react with DHA to produce more melanoidins. However, as the pH increases from 6.2 to 7.4, the browning intensity of all three AA-DHA declines gently. This is due to the fact that DHA is typically stable between pH4 and pH6, but its efficacy is lost with the formation of melanoidins at neutral or higher pH. In addition, the variation of pH also changes the maximum absorption wavelength (λ_{max}) of His-DHA and Lys-DHA, for example, the λ_{max} of His-DHA with 379 nm and Lys-DHA with 371 nm at pH4.4 shift to 403 nm and 408 nm at pH6.2, respectively (unpublished observations). The shift of λ_{max} suggests that different chromophores and conjugated systems have been formed in AA-DHA, corresponding to the colour change of their solutions. This phenomenon can be better and more intuitively observed through the changes of *CIE L*a*b** data, mainly reflected in the values of a^* (redness) and b^* (yellowness) in Figure 3(c). At the same time, the high-resolution mass spectrometry of their solutions indicates that many molecules with different molecular weights are formed under different pH conditions (observations to be published separately). These results are in accordance with the pH effect on browning in foods reported elsewhere that pH has a considerable influence on which route that Maillard reaction will take and which products will be formed[8,30].

Temperature, as another important factor affecting Maillard reaction, has been extensively studied in heat treatment of food[31,32]. Unfortunately, the effects of temperature reported by these studies have all been associated with high temperature (usually above 90 °C) and cannot be transferred to the tanning reaction of DHA on human skin (around 37 °C). Figure 4 clearly indicates that increasing reaction temperature significantly promotes the reaction rate and browning intensity of AA-DHA. The effect of such a phenomenon on the colour of progressive browning is reflected in the decrease in lightness (L^*), the significant loss in yellow hues ($+b^*$) and the shift toward red hues ($+a^*$) that is more prominently associated temperature than pH. Besides, the hue shift is more pronounced the higher the temperature is. In order to investigate the potential role that an elevated level of heat may have on creating complex melanoidins containing different chromophores due to different reaction pathways being followed, Arg-DHA, His-DHA and Lys-DHA systems shown in Figure S4 (b) and (c) were diluted (40 times) and their UV-Vis spectra measured and compared with those obtained from shorter reaction times and lower reaction temperatures. It was found that the profiles of the UV-Vis spectra of AA-DHA at the higher temperatures (43 and 50 °C) were similar to those from the lower temperature (36 °C), the main difference being the change in the intensity of absorbance. It was also found that the higher the temperature, the greater the absorbance. In addition, the HPLC analyses of these samples further indicated that, for the same AA-DHA system, higher temperatures did not lead to the generation of product of different colours, but led to an increase in the concentration of the product of the same or similar colour characteristics, thus deepening the colour of the solution (observations to be published in a follow-on paper). In general, compared with the effects of molar ratio, reaction time and pH, temperature has a more pronounced influence on the colour development of DHA tanning reaction.

5. CONCLUSION

In summary, it has been found that during AA-DHA tanning reactions, the colour of the mixture undergoes a series of changes: yellow, then red and finally dark brown. The colour development kinetics of tanning reaction can be effectively characterised by *CIE L*a*b** values. His and Lys reacted with DHA more rapidly than Arg and the difference was obvious at greater molar ratio and longer reaction time, as reflected in the change of yellowness (*b**). Variation in pH leads to the formation of melanoidins containing different chromophores and conjugated systems, thus producing different colours. pH6.2 facilitates the formation of deeper coloured products, but the stability of DHA at various pH should be taken into consideration in applications. Increasing temperature significantly increases the browning intensity, accompanied by reduced lightness (*L**), significant loss in yellow hues (+*b**) and shift toward red hues (+*a**). In the subsequent studies, the authors will explore the possible reaction pathways and main chemical structure of melanoidins with an aim to explain the colour development mechanism of tanning reaction.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at http://pubs.acs.org.

- Experimental design, images of samples and relevant colour characteristics data under different reaction conditions (PDF)

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Funding Sources

This work was funded by the University of Leeds via the Leeds International Doctoral Scholarship (LIDS).

Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENT

The authors thank the University of Leeds for funding the study through the Leeds International Doctoral Scholarship (LIDS), and PZCussons (Manchester, England) for providing DHA solutions and useful discussions.

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