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Collagen peptide provides *Streptomyces coelicolor* CGMCC 4.7172 with abundant precursors for enhancing undecylprodigiosin production

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Abstract

Effective and ecofriendly converting biomass to chemicals is important for sustainable engineering based on the foreseeable shortage of fossil resources. Undecylprodigiosin (UP) is a promising antibiotic, but the direct feeding of pure precursor amino acids makes it costly for large-scale production. Here, collagen peptide (CP), a renewable animal-derived biomass contains abundant precursor amino acids of UP. CP can act as carbon and nitrogen source for the growth of *Streptomyces coelicolor CG*MCC 4.7172. The plant biomasses including soybean meal, wheat bran, and malt extract were unsuitable for UP prodution. However, 365.40 μg/L UP was detected after 24 h in the media containing CP, and its highest concentration reached 1198.01 μg/L. UP was also detected in the media containing meat hydrolysates of domestic animals, but its initial production time was delayed, and final concentration was lower than that in the medium containing CP only. Compared the fermentation performances of CP and other proteins, CP has a special superiority for UP production. These results revealed that UP biosynthesis may be dependent on amino acid availability of substrates and CP is beneficial for UP production because of its specific amino acid composition.

Keywords: Biomass, Collagen peptide, Fermentation, *Streptomyces coelicolor*, Antibiotic, Undecylprodigiosin

1 Introduction

Biomass has attracted significant attention as a sustainable resource because of increasing environmental concerns and decreasing fossil resources [1, 2]. Biomass can be used to produce important chemicals, such as intermediates, bioenergy, and bioactive molecules related to various aspects of human beings [3, 4]. Nowadays, plant biomass has been extensively exploited, whereas animal biomass is largely underutilized despite its enormous potential due to the limitations of low-value conversion approaches [5]. Therefore, developing an effective and ecofriendly strategy for converting animal biomass to high-value products is particularly important.

Antibiotic is an important pharmaceutical used for humans and domestic animals. The majority of clinical antibiotics of natural origin are produced by *Streptomyces* species [6]. As a model organism, *Streptomyces coelicolor* can produce antibiotics mainly including red-pigmented undecylprodigiosin (UP), blue-pigmented Type II polyketide actinordin, and calcium-dependent lipopeptide antibiotic [7]. Especially, great attention was focused on the UP owing to its immunosuppressive and anticancer properties, in addition to antimicrobial activities [8, 9]. Ho et al. [10] have reported that UP can selectively induce apoptosis in human breast carcinoma cells independent of p53. Thus, UP is a promising antibiotic in the pharmaceuticals industry. Current strategies

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to achieve high UP yield include exploitation of new strains by efficient isolation, construction of industrial producers by metabolic engineering, and supplementation of special precursors by direct feeding [11–14]. In fact, exogenous feeding with special precursors is a pioneering approach to improve antibiotic yield during fermentation.

UP is a member of the family of prodiginines, which are structurally characterized by a common pyrrolylpyrromethene skeleton [15]. Precursors of UP mainly includes acetyl-CoA, malonyl-CoA, proline (Pro), glycine (Gly), and serine (Ser) [16]. Acetyl-CoA is generally derived from the degradation pathway of common sugars, lipids and proteins [17]. Moreover, malonyl-CoA can be obtained by the bioconversion of acetyl-CoA with acetyl-CoA carboxylase [18]. Considering the limitation of common substrates, precursor amino acids (AAs), including Gly, Pro and Ser are generally used in exogenous feeding as the nitrogen source for UP biosynthesis. However, pure free AAs are costly for large-scale fermentation. Therefore, a novel resource of precursors should be developed to achieve the cost-effective production of UP.

Collagen I is an abundant renewable animal biomass, which can be easily extracted from the skins, bones, tendons and cartilage of domestic animals [19–21].The collagen triple- helix consists of a repeating $(Gly\text{-}X\text{-}Y)_n$ sequence, and the AAs in the X and Y positions of collagen are generally Pro and hydroxyproline (Hyp), respectively [19, 22, 23]. The fact illustrated that the Gly-Pro-Hyp is the most common triplet in collagen. Collagen peptide (CP), prepared by the hydrolyzation of collagen I, is easier utilized by microorganisms than collagen [24, 25]. Moreover, CP contains abundant Gly and Pro as UP precursors, based on its unique composition of AAs. In particular, Thomas et al. [26] proved that the pyrrolidine ring of Pro can be incorporated into a pyrrole of UP within its biosynthetic pathways. Besides, Ser is also included in CP, which is also a necessary AA for UP biosynthesis. Accordingly, the AAs composition of CP makes it an ideal substrate for UP production.

In the present study, the effects of different CP concentrations on the growth profile of *S. coelicolor* CGMCC 4.7172 (China General Microbiological Culture Collection Center) were investigated. Besides, the UP producing abilities using CP and these plant biomasses were compared. Meanwhile, the influence of CP on the UP production in the media containing soybean meal (SM) and wheat bran (WB) were analyzed, respectively. For comparison, the investigation of antibiotic producing abilities involved in meat hydrolysates of rabbit, beef, mutton, chicken, and duck were also conducted. The fermentation performances using bovine serum albumin (BSA), casein, and keratin as substrates were also investigated to understand the effect of CP.

2 Materials and methods

2.1 Microorganism and raw materials

The *Streptomyces coelicolor* CGMCC 4.7172 utilized in this study was obtained from the China General Microbiological Culture Collection Center (CGMCC). Collagen peptide (CP) was prepared though the enzymatic degradation of collagen I following the method developed in our previous work [25], and its weight-average molecular weight was 2900 Da. Soybean meal (SM), and wheat bran (WB) were friendly offered by Mianyang Habio Bioengineering Co., Ltd. Soybean powder (SP), and the meat of rabbit, beef, mutton, chicken, and duck were purchased from a local vegetable market. Besides, keratin (from wool) was provided by Tokyo Chemical Industry Co., Ltd. Yeast extract and tryptone were obtained from Oxoid (Cambridge, U.K.). Bovine serum albumin (BSA) and other chemicals were provided by Aladdin (Shanghai, China). The undecylprodigiosin (UP) standard for quantitative analysis was purchased from Abcam (Hong Kong, China).

2.2 Media and cultivation conditions

S. coelicolor CGMCC 4.7172 was routinely maintained on glucose-yeast-malt agar containing (*w/v*) 0.4 % glucose, 0.4 % yeast extract, 1.0 % malt extract (ME), 0.2 % $CaCO_3$, and 1.5-2 % agar powder. Moreover, the seed medium was composed of (*w/v*) 3.0 % yeast extract, 3.0 % tryptone, 0.5 % glucose, 0.4 % maltose, 0.2 % $MgSO_4{\cdot}7H_2O$. The spore suspension of *S. coelicolor* was first inoculated into seed culture medium at a final spore count of 2×10^6 spores/mL, and the strain was cultivated for 2 days (d) in an orbital shaker at 30 ℃ and 200 rpm, which served as an inoculum of the different fermentation media. The cells were inoculated into 250 mL flasks containing 120 mL of fermentation media, and cultured at 30 ℃ with shaking at 200 rpm for different time. Moreover, all initial pH values of these fermentation media were adjusted to 7.0-7.2 and followed its natural course.

2.2.1 Effect of different CP concentrations in ISP-2 media

International *Streptomyces* Project medium No.2 (ISP-2) for fermentation was composed of (*w/v*) 0.4 % glucose, 0.4 % yeast extract, and 1.0 % ME. Moreover, different concentrations of CP were separately added into ISP-2 medium to form different fermentation media. The cultivated cells were directly inoculated at a concentration of 5 % (*v/v*) into these media.

2.2.2 Comparison of CP with other biomasses

The minimal medium (MM), including (*w/v*) 0.05 % KH_2PO_4, 0.15 % Na_2HPO_4, 0.10 % NaCl, and 0.02 % $MgSO_4{\cdot}7H_2O$, was used as basal culture media. Furthermore, CP and other various substrates were added into MM media to form different culture media. The cultivated cells in seed media were collected, washed, and re-suspended in equal volume of sterile 0.85 % (*w/v*) NaCl. The prepared cells were inoculated at a concentration of 5 % (*v/v*) in different culture media.

2.3 Analytical methods

An aliquot of *S. coelicolor* CGMCC 4.7172 culture was harvested by centrifugation, and then suspended in 0.5 mol/L HCl methanol for UP extraction. The UP concentration was analyzed by high-performance liquid chromatography (HPLC, Agilent 1260 Infinity, Agilent Technologies, SantaClara, US-CA) with a Zorbax Eclipse Plus C18 column (250 × 4.6 mm, i.d.; 5 μm) and a diode-array detector. The column temperature was 30 ℃ with a constant flow rate at 0.6 mL/min and an absorbance at 530 nm. The mobile phase was a gradient prepared from methanol (A) and 0.1 % formic acid in water (B) according to the following program: 0–10 min, 5–100 % A; 10–18 min, 100 % A; 18–20 min, 100–5 % A; 20–25 min, 5 % A.

The carbon-to-nitrogen (C/N) ratio of the substrates were calculated by measuring their content of C and N using a Flash EA 1112 NC analyzer (Thermo Fisher Scientific Inc., Waltham, MA, USA) [27, 28]. Besides, the amino acids (AAs) compositions of these substrates were determined by an A300 fully automatic AA analyzer (Membrapure, Berlin, Germany) [29]. These substrates were hydrolyzed with 6 mol/L HCl at 120 ℃ for 24 h, and the hydrolysates were used to analyze the contents of the corresponding AAs [30]. In addition, the cell growth was characterized as dry cell weight (DCW). The cell pellets in an aliquot culture were collected, washed, and then dried at 55 ℃, until the weight remained stable [31]. Meanwhile, the contents of total organic carbon (TOC) and total chemically bound nitrogen (TNb) of the culture supernatant during fermentation were measured using a C and N analyzer (Vario TOC, Elementar, Hanau, Germany) [32, 33].

2.4 Effect of CP on the growth profile of the *S. coelicolor*

2.4.1 Effect of different CP concentrations

ISP-2 media were supplemented with 0.1 %, 1 %, 2 %, 3 %, 4 %, and 5 % (*w/v*) CP and labeled as ISP-2_0.1CP, ISP-2_1CP, ISP-2_2CP, ISP-2_3CP, ISP-2_4CP and ISP-2_5CP media, respectively. The cultivated cells were directly inoculated to these media to explore the influence of CP concentrations on the growth of *S. coelicolor*. The pH value and DCW were determined during the fermentation period of 13 d.

2.4.2 Growth profile of *S. coelicolor* when CP acted as the sole source of carbon and nitrogen

MM medium, containing only inorganic salt without any source of carbon and nitrogen, was served as control. According to the pre-experimental results (Supplementary Note 1, and Fig. S1a and b), the concentration of CP was determined as 2 % (*w/v*) to investigate the fermentation performances of *S. coelicolor*. Thus, the prepared cells, almost without the components of seed media, were inoculated into the MM and 2CP (MM media containing 2 % (*w/v*) CP) media to investigate the growth behavior of the *S. coelicolor*, when CP was used as the sole source of carbon and nitrogen. The pH values and DCW were tested during the culture period.

2.5 Comparison of UP biosynthesis performance between CP and plant biomass

2.5.1 UP producing abilities of CP and plant biomass

MM media were separately supplemented with (*w/v*) 2 % SM, 2 % SP, 2 % WB, and 2 % ME, and designed as 2SM, 2SP, 2WB and 2ME media, which were used to compare the UP producing abilities between CP and plant biomass. The UP concentration was measured during the fermentation period of 13 d. Moreover, the CP concentration added in MM media was increased to 4 % (*w/v*), which was designed as 4CP media. Meanwhile, the added concentration of plant biomass was also doubled, and the fermentation period was prolonged to 20 d for gaining insight into the difference of UP producing ability between CP and the four plant biomasses. The MM media containing (*w/v*) 4 % SM, 4 % SP, 4 % WB, and 4 % ME were labeled as 4SM, 4SP, 4WB, and 4ME media, respectively. In addition, the Pro, Gly and Ser contents of the biomass resources, including CP, SM, SP, WB, and ME, were analyzed.

2.5.2 Effect of CP on UP fermentation

MM media supplemented with (*w/v*) 2 % SM and 2 % CP was deemed as 2SM_2CP media. Similarly, MM media containing (*w/v*) 2 % WB and 2 % CP was denoted as 2WB_2CP media. The pH value and UP concentration were measured to evaluate the effect of CP on fermentation by the strain *S. coelicolor*.

2.6 Fermentation performance of meat hydrolysates by *S. coelicolor* CGMCC 4.7172

Meat hydrolysates were prepared by the enzyme hydrolysis of rabbit, beef, mutton, chicken, and duck as previously described [25]. The 2 % (*w/v*) meat hydrolysate of rabbit, beef, mutton, chicken, and duck were contained in MM media, respectively. The C/N ratios of

these substrates were analyzed. Meanwhile, the contents of hydroxyproline (Hyp) included in CP and these animal biomasses were determined. In addition, the pH value and UP concentration were measured during the fermentation period of 20 d.

2.7 UP producing ability of animal protein

MM media including (*w/v*) 2 % BSA, 2 % casein, and 2 % keratin were used to study the antibiotics producing ability of animal protein. The contents of Pro, Gly, and Ser and the C/N ratio of these substrates were analyzed. In addition, the pH value and UP concentration were measured during the fermentation period of 20 d.

2.8 Statistical analysis

Data were subjected to statistical analysis performed by SPSS (version 25.0 for windows, SPSS Inc., CO, USA) and graphs were created in Origin Pro 2017 (Origin Lab Corporation, Northampton, MA, USA). The results were expressed as mean ± standard deviation (SD). One-way ANOVA with Tukey's HSD analysis were used to determine significance, and the level of significance was $p < 0.05$.

3 Results and discussion

3.1 Effect of CP on the growth profile of the *S. coelicolor*

The different concentrations of CP were added into ISP-2 media to investigate the effect of CP addition on the growth of *S. coelicolor* CGMCC 4.7172. Actually, ISP-2 and YEME media are the common media for cultivating *S. coelicolor* [34–36]. It was found that the *S. coelicolor* in ISP-2 media had higher UP concentration but lower DCW than those in YEME media (Supplementary Note 1, and Fig. S1a and b). Hence, ISP-2 medium was used as a probe medium for further investigation of growth.

In general, the DCW of the *S. coelicolor* increased with the addition of CP (Fig. 1a). The highest DCW was reached at 5 d in ISP-2 media with 3.17 g/L, while the DCW increased to 4.40, 8.02, and 15.90 g/L in ISP-2_1CP, ISP-2_3CP, and ISP-2_5CP media at 3 d, respectively. Besides, the second growth of *S. coelicolor* was observed when more than 1 % (*w/v*) CP was added, and the highest DCW was obtained in ISP-2_5CP at 13 d among these media. These results suggest that addition of CP can promote the growth of *S. coelicolor*. Moreover, pH is a comprehensive index reflecting the metabolic activity of microorganism [37]. At the early fermentation stage,

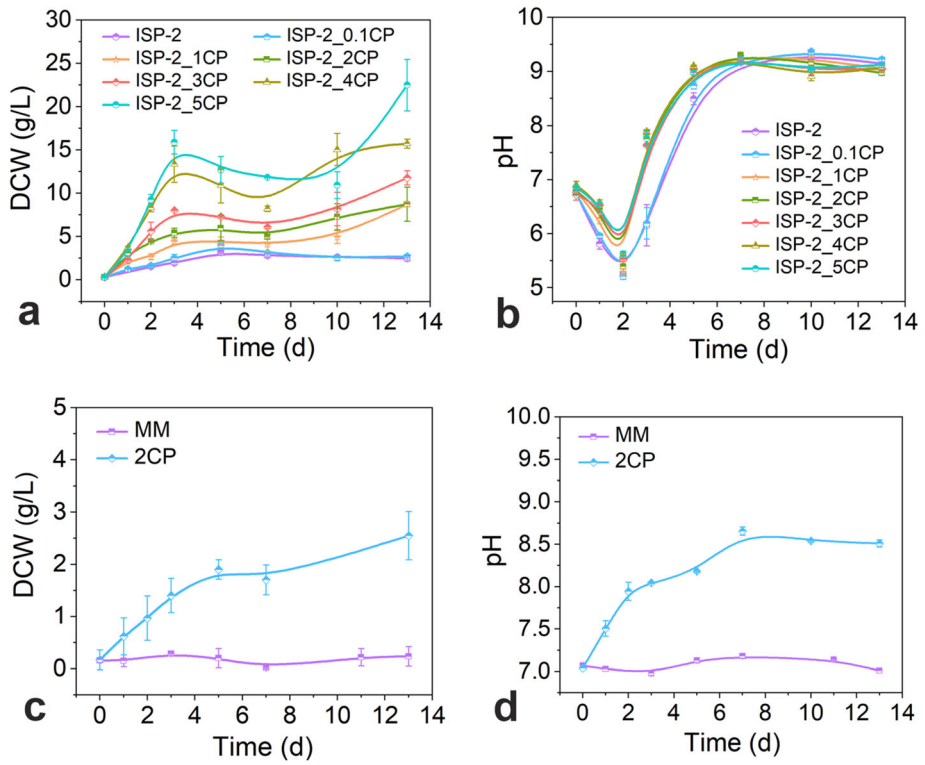

Fig. 1 Influence of CP on the growth behavior of the strain *S. coelicolor* CGMCC 4.7172. **a** and **b** Time course of DCW and pH values in the ISP-2, ISP-2_0.1CP, ISP-2_1CP, ISP-2_2CP, ISP-2_3CP, ISP-2_4CP and ISP-2_5CP media, respectively. **c** and **d** The change of DCW and pH values in the MM and 2CP media during the culture process of 13 d, respectively

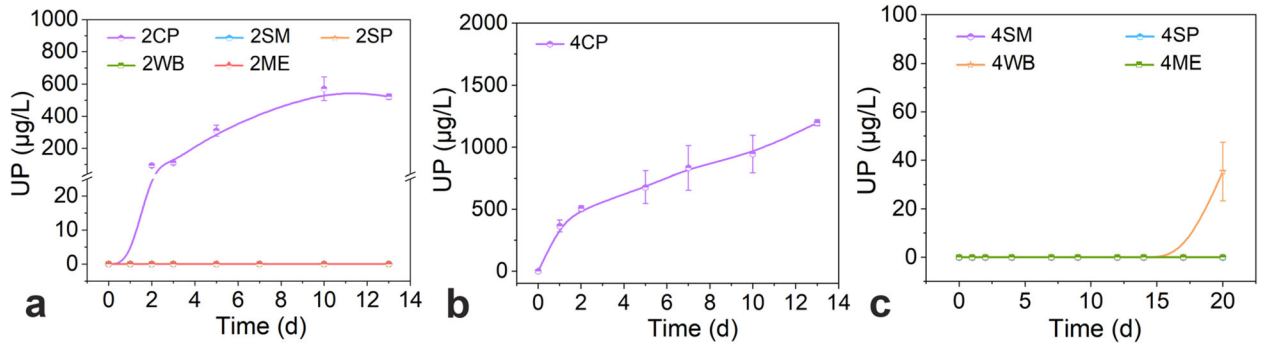

Fig. 2 Comparison of UP producing ability between CP and plant biomass by *S. coelicolor* CGMCC 4.7172. **a** The UP concentrations in the 2CP, 2SM, 2SP, 2WB and 2ME media, respectively, during the fermentation process of 13 d. **b** The UP concentrations in the MM media supplemented with 4 % (*w/v*) CP (4CP media). **c** The UP yields in 4SM, 4SP, 4WB, and 4ME media, respectively, during the fermentation period of 20 d

the pH values were elevated when CP was added (Fig. 1b), which indicated that the existence of CP can change the metabolism of *S. coelicolor*, thereby increasing pH values.

Furthermore, the TOC and TNb of the fermentation broth increased, whereas the TOC/TNb declined with increasing CP concentration (Fig. S2), because CP also belongs to protein-based biomass. The strain *S. coelicolor* showed poor growth in MM media, which only contained inorganic salts without any carbon and nitrogen sources (Fig. 1c). However, when 2 % (*w/v*) CP was added into MM media, the *S. coelicolor* exhibited normal growth during the culture

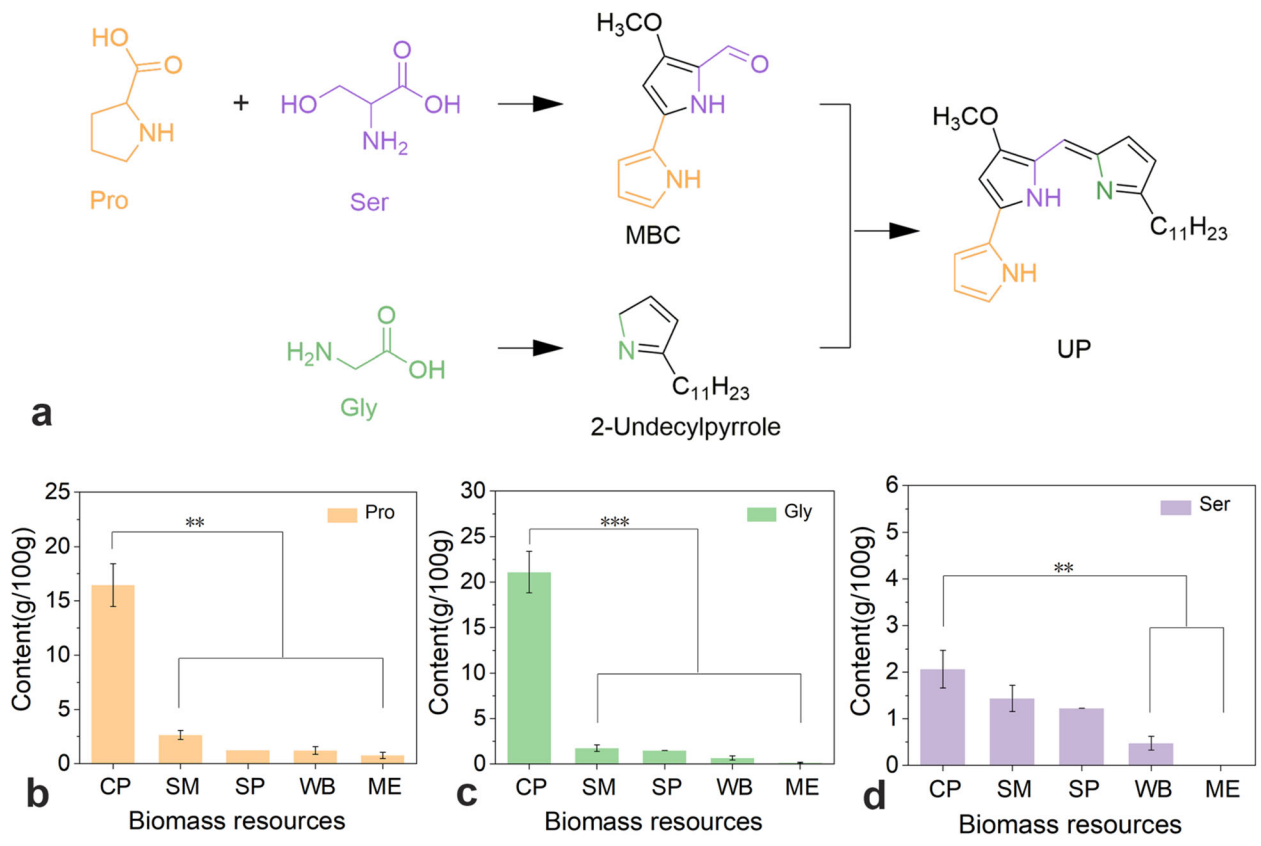

Fig. 3 UP precursor AAs, and their contents in CP and common plant biomass. **a** The structures of UP, precursor AAs and intermediates. Each color shows a different initial precursor amino acid. **b-d** The contents of Pro, Gly, and Ser in the biomass resources of CP, soybean meal (SM), soybean powder (SP), wheat bran (WB) and malt extract (ME), respectively. MBC: 4-methoxy-2,2′-bipyrrole-5- carbaldehyde. *P* values represent levels of significant ($p < 0.001$ ***, $p < 0.01$ **, $p < 0.05$ *)

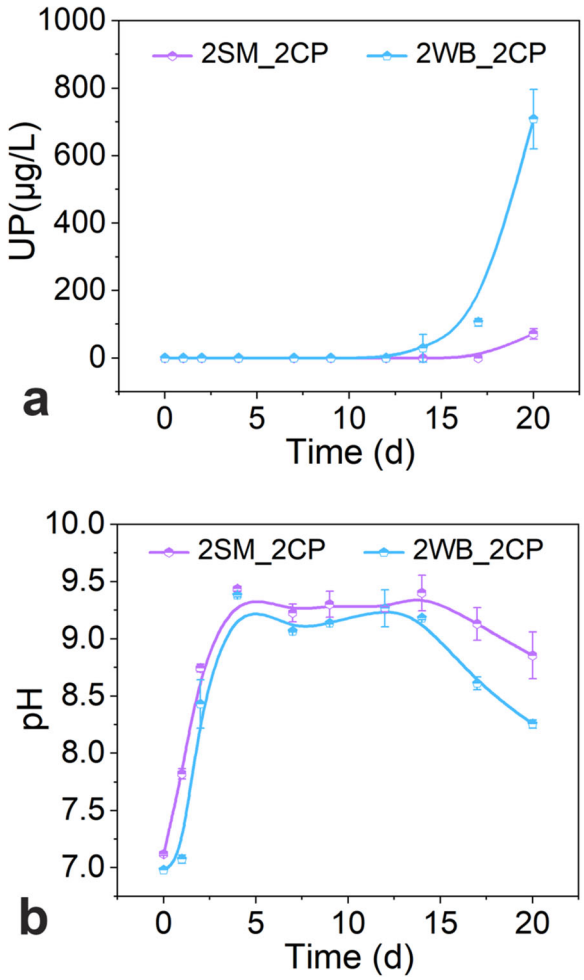

Fig. 4 Effect of CP on fermentation performance of *S. coelicolor* CGMC C 4.7172. **a** and **b** The variation of UP concentrations and pH values in 2SM_2CP and 2WB_2CP media, respectively, during the fermentation process of 20 d

process. The results suggest that CP can be used as a carbon and nitrogen source for the growth of *S. coelicolor*. In addition, the pH values in MM media were almost unchanged throughout the fermentation period of 13 d (Fig. 1d). However, when CP was added into MM media, the pH values increased from the initial pH 7.04 to the peak of 8.66 at 7 d, which further demonstrated that CP can be utilized by the *S. coelicolor*.

3.2 Comparison of UP biosynthesis performance between CP and plant biomass

3.2.1 UP producing abilities of CP and plant biomass

Zang et al. [38] reported that the C/N ratio of the media is critical for *Serratia marcescens* N10612 to produce prodigiosin isoform pigment. These plant biomasses with different C/N ratios (Fig. S3) were separately added into MM media for the comparison with CP on antibiotic production. Virtually, SM, SP, WB, and ME are prevalent plant biomasses used in the fermentation industry. Surprisingly, UP was not detected in the 2SM, 2SP, 2WB, and 2ME media during the whole fermentation period of 13 d (Fig. 2a). However, the UP concentration in the MM media with 2 % (*w/v*) CP was 93.06 μg/L at 2 d, and then it increased to 571.94 μg/L after 10 d. These results indicated that CP can be both used as carbon and nitrogen sources to produce UP.

Intriguingly, when the CP concentration increased from 2 to 4 % (*w/v*), the UP was detected after 24 h with 365.40 μg/L, and it reached the highest concentration at 13 d with 1198.01 μg/L (Fig. 2b). Moreover, the concentrations of plant biomasses also increased to 4 % (*w/v*) for investigating the antibiotic producing abilities of *S. coelicolor* CGMCC 4.7172 in 4SM, 4SP, 4WB and 4ME media. It was found that only a small amount of UP was produced in 4WB media, and no UP was detected in other media, even though the fermentation time was prolonged to 20 d (Fig. 2c). These results suggested that SM, SP, WB and ME are not suitable for the strain to produce UP, while CP can enhance UP production.

It was reported that the biosynthesis of antibiotics in *S. coelilcolor* is greatly affected by precursor supply [39]. Stankovic et al. [11] have reported that the cell dry weight and UP concentration were increased by 1.46 and 1.49 folds, respectively, when MSY media was supplemented with (*w/v*) 0.1 % Pro, 0.1 % Gly and 0.1 % Ser. Wei et al.[40] have reported that UP concentration increased to 2.90 folds when 0.5 % (*w/v*) Pro was added into LB media by *Serratia marcescens* Simon Swift-1 (SS-1), suggesting that the addition of precursor amino acids can enhance UP production. UP is a tripyrrole antibiotic, which is condensed by two intermediates, 2-undecylpyrrole and 4-methoxy-2,2′-bipyrrole-5-carbaldehyde (MBC) [41] (Fig. 3a). Basically, the N contained in UP tripyrrole structure is obtained from Pro, Gly, and Ser, respectively [16, 42]. Hence, Pro, Gly, and Ser are essential precursor AAs for UP biosynthesis.

Interestingly, the contents of Pro, Gly, and Ser in CP are the highest among these biomass resources, which are roughly 16.45, 21.10, and 2.06 g/100 g CP, respectively (Fig. 3b-d). The contents of Pro in ME, Gly in SM, and Ser in WB are only approximately 1/21, 1/12, and 1/4 folds those in CP, respectively. Thus, a possible explanation for the stimulation of UP production could be the increased precursor availability due to CP supplementation.

3.2.2 Effect of CP on UP fermentation

UP yield increased when SM and WB in 4SM and 4WB media were partly replaced by CP (Fig. 2c and 4a). Surprisingly, the UP concentration increased from 35.37 μg/L in 4WB media to 708.60 μg/L in 2WB_2CP media at 20 d. Meanwhile, 71.13 μg/L UP concentration was detected at 2SM_2CP media after fermentation. Besides, the pH values in 2SM_2CP and 2WB_2CP media increased with the increase of time at the early fermentation stage (Fig. 4b), indicating that the nutrients of the media were utilized by the strain *S. coelicolor*. These results revealed that CP supplementation contributed to the increase in UP yield, and the biosynthesis of UP may be dependent on AA availability of substrates.

3.3 Comparison of fermentation performances between CP and meat hydrolysates

The hydrolysates of rabbit, beef, mutton, chicken, and duck meats were also added into MM media to compare the fermentation performances of CP with meat hydrolysates by *S. coelicolor* CGMCC 4.7172. Compared with the above plant biomass, the C/N ratios of the chosen meat hydrolysates are relatively closer to each other, ranging from 3.54 of duck to 4.30 of rabbit (Fig. 5a). Moreover, the pH values in the MM media containing the five meat hydrolysates all increased with fermentation time at the early fermentation stage, and then almost remained unchanged (Fig. 5b). These facts illustrated that these meat hydrolysates can be utilized by *S. coelicolor*.

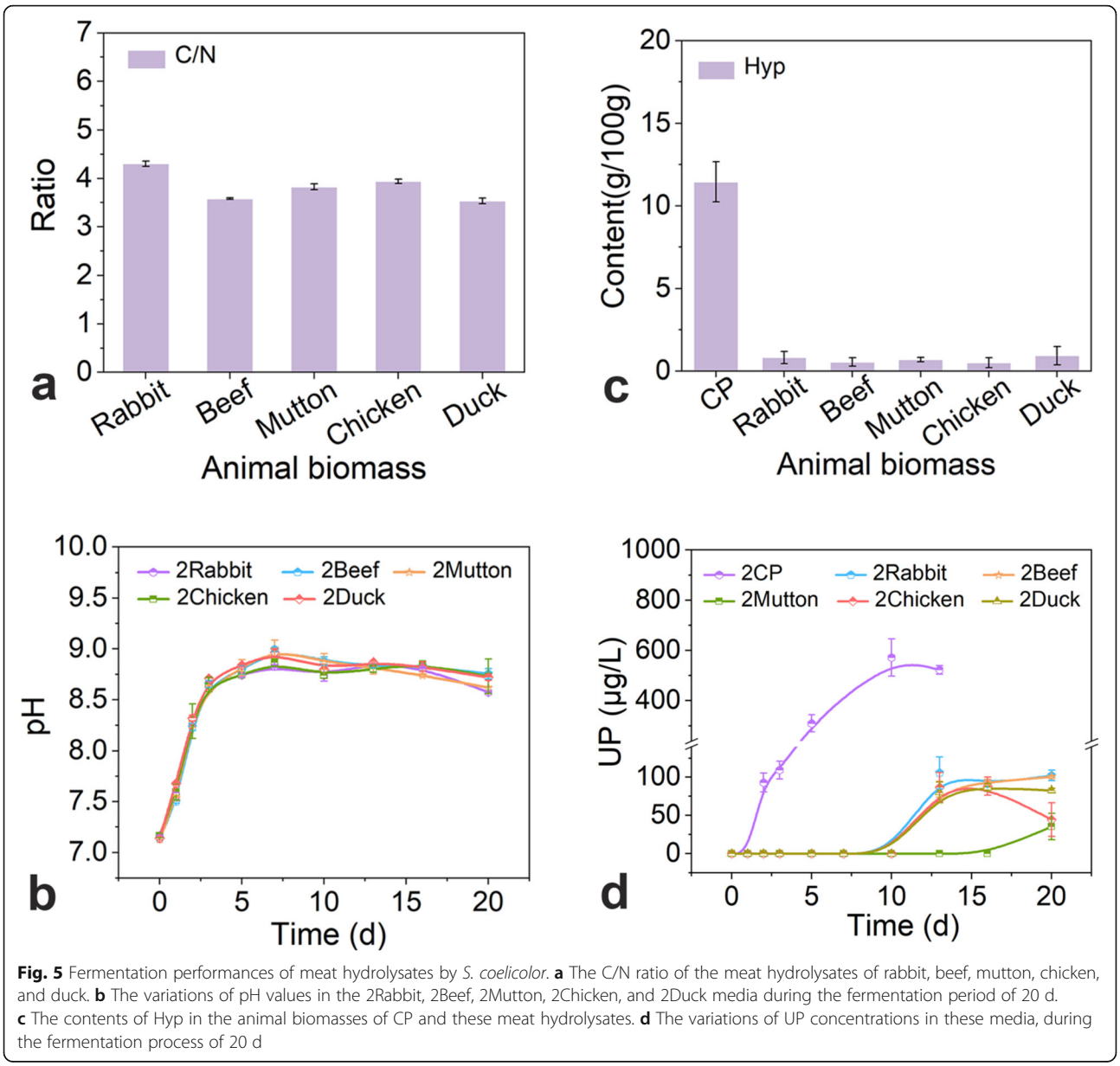

Fig. 5 Fermentation performances of meat hydrolysates by *S. coelicolor*. **a** The C/N ratio of the meat hydrolysates of rabbit, beef, mutton, chicken, and duck. **b** The variations of pH values in the 2Rabbit, 2Beef, 2Mutton, 2Chicken, and 2Duck media during the fermentation period of 20 d. **c** The contents of Hyp in the animal biomasses of CP and these meat hydrolysates. **d** The variations of UP concentrations in these media, during the fermentation process of 20 d

Actually, Hyp is a characteristic AA of collagen, and its content in the CP is up to 11.45 g/100 g (Fig. 5c). Meanwhile, a small amount of Hyp was detected in the five meat hydrolysates. It was noted that the stain *S. coelicolor* cultured in the MM media containing these meat hydrolysates all produced UP during the fermentation period of 20 d (Fig. 5d), but the UP yields were significantly lower than that in CP containing media. These results illustrated that CP may drive the nutrient catabolism toward an increased supply of precursors, which can directly participate in UP biosynthesis.

However, UP was detected until 13 d in the MM media with the meat hydrolysates of rabbit, beef, chicken, and duck. Besides, the highest UP concentrations were 105.70, 100.64, 35.54, 88.36 and 86.83 μg/L in the 2Rabbit, 2Beef, 2Mutton, 2Chicken, and 2Duck media, respectively. Obviously, the initial producing time was delayed and the final UP concentration was lower in these media, in comparison with that in 2CP media. Therefore, it is reasonable to believe that CP has a special superiority for UP production due to its unique AAs composition.

3.4 UP producing ability of animal proteins by *S. coelicolor*

The importance of amino acids composition of substrates to produce UP was further analyzed. BSA, casein, and keratin were selected to supplement in MM media for exploring their antibiotic producing abilities, when they acted as a sole source of carbon and nitrogen fermented by *S. coelicolor* CGMCC 4.7172. Actually, the C/N ratios of BSA, casein, and keratin showed no obvious differences at 3.44, 3.71, and 3.15, respectively (Fig. 6a). The main chemical compositions of BSA, casein and keratin are summarized in Table S1. The content of Ser was higher, while the contents of Pro and Gly were evidently lower in BSA, casein, and keratin than those in CP (Fig. 6b- d). In particular, the Gly contents were the lowest among the three AAs for each of the animal proteins.

Fermentation experiments showed the UP was not detected in 2BSA, 2Casein, and 2Keratin media during the fermentation period of 20 d (Fig. 6e), possibly due to the limitation of Gly. Actually, Gly is an essential

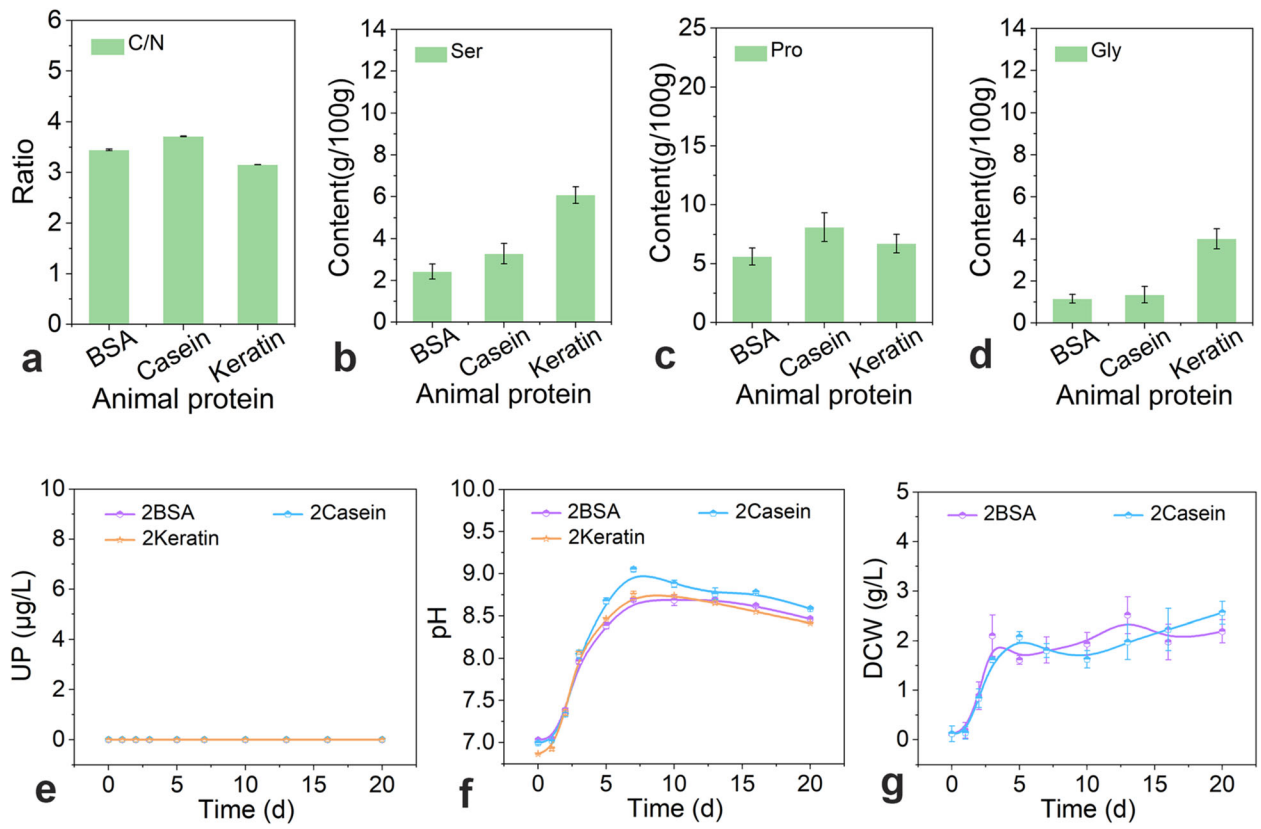

Fig. 6 The AAs characteristics and UP producing ability of the animal proteins by *S. coelicolor*. **a** The C/N ratio of the animal proteins including BSA, casein, and keratin. **b**-**d** The contents of Ser, Pro, and Gly in the three animal proteins, respectively. **e** and **f** The variations of UP concentrations and pH values in the 2BSA, 2Casein, and 2Keratin media, respectively, during the fermentation period of 20 d. **g** The change of DCW in the 2BSA and 2Casein media during the fermentation process

component to the structure of 2-undecylpyrrole, which was an intermediate for UP biosynthesis [41, 43]. In fact, the pH changes in these media were basically consistent with those in MM media containing meat hydrolysates (Fig. 5b and 6f). The highest pH values were reached at 7 d with 8.69, 9.05 and 8.76 in the 2BSA, 2Casein, and 2Keratin media, respectively. In particular, the DCW increased with the prolonged time at the early fermentation stage in the 2BSA and 2Casein media (Fig. 6g), indicating the animal proteins were utilized for the growth of *S. coelicolor* rather than contributing to UP production. These results further demonstrated that the UP production of *S. coelicolor* is closely related to the AA composition of the substrates, and that CP has a high content of precursor AAs needed for UP biosynthesis.

4 Conclusions

This study provides novel insights regarding the application of animal biomass CP and the development of raw stock sources for UP production. The addition of CP can boost the growth of *S. coelicolor* CGMCC 4.7172. Meanwhile, CP can be used as carbon and nitrogen source for the growth and antibiotic production of *S. coelicolor*. Plant biomasses including SM, SP, WB and ME were unsuitable for producing UP, whereas CP can promote UP production. Compared with other animal biomass, CP is a promising biomass resource to produce UP because of its specific AA composition. In future investigations, the application behaviors of CP in large-scale UP production and other high value-added products by fermentation are worth anticipated.

Abbreviations

CP: Collagen peptide; UP: Undecylprodigiosin; *S. coelicolor*: *Streptomyces coelicolor*; Pro: Proline; Gly: Glycine; Ser: Serine; AAs: Amino acids; Hyp: Hydroxyproline; CGMCC: China General Microbiological Culture Collection Center; BSA: Bovine serum albumin; SM: Soybean meal; WB: Wheat bran; SP: Soybean powder; ME: Malt extract; ISP-2: International *Streptomyces* Project medium No.2; HPLC: High-performance liquid chromatography; C/N: Carbon-to-nitrogen ratio; DCW: Dry cell weight; TOC: Total organic carbon; TNb: Total chemically bound nitrogen; MM: Minimal medium; MBC: 4-methoxy-2,2′-bipyrrole-5-carbaldehyde

5 Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s42825-021-00059-y.

Additional file 1: Supplementary Note 1. Comparison of fermentation performance in the common fermentation media by *Streptomyces coelicolor* CGMCC 4.7172. **Figure S1.** Comparison the fermentation performances of *S. coelicolor* CGMCC 4.7172 cultured in ISP-2 and YEME media for 7 d. **Figure S2.** The change of TOC and TNb in ISP-2 media with different CP concentrations fermented by *S. coelicolor* CGMCC 4.7172. **Figure S3.** The C/N ratio of the biomass substrates including collagen peptide (CP), soybean meal (SM), soybean powder (SP), wheat bran (WB) and malt extract (ME). **Table S1.** The mainly chemical compositions of BSA, casein and keratin.

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Authors' contributions

Xia Li: Conceptualization, Methodology, Investigation, Writing - original draft. Meifeng Li: Investigation, Data curation. Junling Guo: Methodology. Xian Liu: Formal analysis. Xuepin Liao: Conceptualization, Methodology, Supervision, Writing - review & editing. Bi Shi: Conceptualization, Supervision. The author(s) read and approved the final manuscript.

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Availability of data and materials

All data generated or analyzed during this study are included in this manuscript and additional file.

Declaration

Competing interests

The authors declare that they have no competing interests.

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